Clinical Features of Dengue Infection in Hospital for Tropical Diseases, Thailand

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Author’s contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Background: Dengue infection is the common infectious disease in tropical countries caused by dengue virus, which has four serotypes (DEN 1, 2, 3 and 4). More data showed that dengue has caught worldwide attention due to its severe and fatal clinical outcome. This study aimed to describe the difference of clinical features of dengue infection between children and adults and among each dengue serotypes in Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand during 2011-2013.

Study Design: This study was a hospital-based retrospective. In-patient medical record of 50 children and 148 adults with clinical and laboratory confirmed dengue infection and admitted to Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand during July 2011-June 2013 were reviewed.

Results: We found that headache and myalgia/arthalgia were found in most of the cases (182/198, 91.9%, 178/198, 89.9%, respectively). Epistaxis and hypermenorrhea were more common in children. Retro-orbital pain was more common in adult. The spontaneous bleeding tended to be more common in children than adults. DEN2 (48.9%) was the most common serotype followed by DEN3 (23.7%), DEN1 (22.2%) and DEN4 (5.2%). Regarding dengue serotypes, subjects infected with DEN1 had more shock, hypermenorrhea and epistaxis than others. Lymphadenopathy and

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rash during febrile stage were found in subjects infected with DEN2 only. Subjects infected with DEN4 infection had more retro-orbital pain and petechiae than others.

**Conclusion:** The results show secondary dengue infection was most common and the most prevalent dengue serotype was serotype 2. Typical symptoms in adult involved retro orbital pain, nausea and arthralgia while children might suffer epistaxis and hypermenorrhea. We also found that DEN 1 tended to have more mucosa bleeding and shock. In DEN 4 infection, subjects had more retro-orbital pain and skin bleeding.

**Keywords:** Dengue infection; dengue serotypes; clinical features; children; adult.

## 1. INTRODUCTION

Dengue infection is the common infectious disease in tropical countries caused by dengue virus, which is a single stranded RNA virus. *Aedes aegypti* is a mosquito, which can transmit the viruses that cause dengue fever confirmed by John Burton and Joseph Franklin Siler in 1907 [1]. The symptoms of dengue fever include fever, headache, muscle and joint pains, and a characteristic skin rash. The first case report of dengue fever is described in a Chinese medical encyclopedia (265-420AD), which referred it as a "water-poison" associated with flying insects [2]. Impact of globalization has led to the spread of *Aedes aegypti* out of Africa during the period between 15th and 19th century [3]. In 1977, DENV 1 was introduced, while both DENV 2 and DENV 4 caused endemics in 1981 and 13 years later outbreak of DENV 3 occurred [4,5]. Dengue is becoming endemic in more than 125 countries and is currently regarded as a worldwide problem [6]. It is estimated that 50 million dengue infections occur annually and up to 3.6 billion people are estimated to live in tropical and subtropical areas, which favor dengue viruses transmission [5,7,8]. Rapid urbanization in Asia and Latin America is being cited as leading causes of endemicity of dengue as crowded urban population facilitates the creation of favorable breeding cites for mosquitoes. Dengue infections in Africa remain underreported, however, recent outbreaks suggest that substantial parts of the continent may be at risk for increasing dengue transmission. More surveillance is needed to determine the epidemiology and true incidence of dengue in Africa [6].

Nowadays, dengue has caught worldwide attention due to its severe and fatal clinical outcome [9]. It is estimated that 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries [10]. In 2007, Gulati and Maheshwari published the atypical manifestations of dengue and classified as neurological, gastrointestinal, cardiovascular, renal, respiratory, and lymphoreticular manifestations [11]. Among them, the common manifestation is encephalopathy with ratio of cases per 1000 people with dengue hemorrhagic fever was 177 in Indonesia in 1975 to 1977 [12], 8 in Thailand in 1995, 5 in Vietnam in 1999 [13,14]. Other manifestations were acute respiratory distress syndrome and acalculous cholecystitis [15]. Dengue infection was thought to be a disease that mainly affected children. However, some studies have reported that the age distribution of this disease has shifted to older age groups [8].

Therefore, the significance of this study was to describe different clinical manifestations of dengue in children and adults. This study aimed to provide clinicians and researchers to get better awareness about dengue infection and hope that deeper understanding about this disease would help the health care providers and researchers to engage better management of dengue infection in the future.

## 2. MATERIALS AND METHODS

### 2.1 Study Population

This retrospective study was based on Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand during July 2011 to June 2013. We collected data from the medical records of dengue patients who were admitted to hospital. The inclusion criteria were patients with clinical dengue infection admitted to hospital and serological or virological confirmation of dengue infection (positive Dengue IgM, PCR for Dengue, Dengue NS1 or increased Dengue antibody titer). The exclusion criteria were no medical record available and patients with co-infection. Among them, only 198 that met the inclusion and exclusion criteria. The data entry form recorded demographic data, medical history, signs of bleeding, laboratory findings, treatment and
confirmed laboratory results (NS1, PCR and ELISA).

2.2 Definitions

Patient < 18 years of age were considered children and adult were defined as ≥ 18 years. The clinical diagnosis was classified according to WHO criteria [10], dengue fever (DF) was defined as presence of fever and two or more of the following, retro-orbital or ocular pain, headache, rash, myalgia, arthralgia, leukopenia, or hemorrhagic manifestations (e.g. positive tourniquet test, petechiae; purpura/ecchymosis; epistaxis; gum bleeding; blood in vomitus, urine, or stool; or vaginal bleeding) but not meeting the case definition of dengue hemorrhagic fever. Anorexia, nausea, abdominal pain, and persistent vomiting may also occur but are not case-defining criteria for DF. Dengue hemorrhagic fever (DHF) was defined as Fever lasting from 2-7 days, evidence of hemorrhagic manifestation or a positive tourniquet test, thrombocytopenia (≤100,000 cells per mm3), evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit ≥ 20% above average for age or a decrease in hematocrit ≥ 20% of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoproteinemia. Dengue shock syndrome (DSS) defined as all criteria for DHF plus circulatory failure as evidenced by: rapid and weak pulse and narrow pulse pressure (>20mm Hg) or age-specific hypotension and cold, clammy skin and restlessness.

2.3 Laboratory Test for Confirmatory of Dengue Infection

The most commonly used method for diagnosing dengue infection is an enzyme-linked immunosorbent assay (ELISA) and it was the diagnostic choice [16]. The serum samples were taken from the patient and tested for anti-dengue virus IgM and IgG and interpreted the ratio of anti-dengue IgM to IgG. If IgM and IgG ratio is more than reference cut off value, regarded as primary infection while the secondary infection occurs cut off point level become lower [17]. Other laboratory techniques include detection of RNA using reverse transcriptase polymerase chain reaction (RT-PCR) and viral isolation. These two tests were effective during the first five days of fever [17]. In 2008, modified nested serotype-specific RT-PCR was developed [18]. Dengue virus non-structural protein-1 (NS1) was initially introduced in year 2000. NS1 is detectable in acute phase of both primary and secondary dengue infection [19]. NS1 level in primary dengue infection had high around day 4 – 5 in early febrile period, and decreased rapidly from day 4–5 onward in secondary dengue infections [7].

2.4 Statistical Analysis

Clinical data were described using descriptive statistics such as mean or median for continuous variables, and percentage for categorical variables. Clinical features & outcome difference of dengue between children (aged <18 years) and adults (aged 18 years or more) were compared using Chi-square test/ Fisher-exact test for categorical variables and T test for continuous variable. For comparing difference among each dengue serotype, we used Chi-square test/ Fisher-exact test for categorical variables and T test for continuous variable. The level of statistical significance was accepted at p-value < 0.05.

2.5 Ethics Committee Approval

This study was approved by the Ethics Committee, Faculty of Tropical Medicine, Mahidol University.

3. RESULTS

Among 198 inpatient medical records of patients with dengue infection, 105 were males with ratio of male: female in both children and adults were 1.1:1. Among 50 cases of children (aged 2 - 18 years), most of them were >9-18 years (46, 88%). Among 148 cases of adults (aged > 18 years), the majority of cases in adults were in 19-30 years old (88/158, 59.5%), while the minorities of cases in adults (5/158, 3.4%) were above 60 years old. Most subjects had normal nutritional status 31/52 (62.0%) in children and 71/148 (48.0%) in adults. There were only 2 (1.4%) obese adults. There were 27 adult cases of hypertension with good response to anti-hypertensive. Aside from this, one child and one adult with asthma were reported (Table 1).

Characteristics of dengue infection between age groups Dengue fever (DF) was the most common clinical diagnosis in both children and adults (72% and 70.3%, respectively) Dengue shock syndrome were found in 4 (8%) children and 6 (5.1%) adults. From 131 available data, 97% of children and adults had secondary infection. Dengue serotype 2 DEN2 (66/135,
48.9%) was the most common serotype in both children and adults (44.1% and 50.5%, respectively) followed by DEN3, DEN1 and DEN 4 (23.7%, 22.2%, and 5.2% respectively) (Table 2).

Regarding signs and symptoms of dengue infection, headache was the most common symptom (94% in children and 91.2% in adult), followed by myalgia/arthritisgia (92% in children and 89.2% in adults) and nausea/vomiting (74% in children and 76.4% in adults). There was no difference in clinical manifestations between both groups except retro-orbital pain and spontaneous bleeding. Retro-orbital pain was more common in adults with odds ratio of 0.46. The spontaneous bleeding tended to be more common in children than adults (48% VS 41.2%, respectively). Epistaxis and hypermenorrhea were more common in children with odds ratio of 2.63 and 4.20, respectively (Table 3).

DHF was more common in DEN 2 infection (36.4%), followed by DEN 3, DEN 4 and DEN 1 (31.2%, 28.6% and 26.7% respectively). There was no case of dengue shock syndrome in DEN 4 infection (Table 4).

Regarding dengue serotypes, subjects infected with DEN1 had more shock (10.0%), hypermenorrhea (44.4% in female aged>10 years), and epistaxis (13.3%) than others. Lymphadenopathy (3.0%) and rash during febrile stage (3.0%) were found in subjects infected with DEN2 only. Subjects infected with DEN4 infection had more retro-orbital pain (85.7%) and petechiae (28.6%) than others (Table 5).

Table 1. Demographic data of subjects by age groups

| General profiles [n (%)] | Children (n= 50) | Adults (n= 148) |
|-------------------------|-----------------|----------------|
| **Gender**              |                 |                |
| Male                    | 27 (54.0)       | 78 (52.7)      |
| Female                  | 23 (46.0)       | 70 (47.3)      |
| **Age (years)**         |                 |                |
| 2 – 9                   | 4 (8.0)         |                |
| >9 – 18                 | 46 (82.0)       |                |
| >18 – 30                |                 | 88 (59.5)      |
| >30 – 40                |                 | 36 (24.3)      |
| >40 – 50                |                 | 9 (6.1)        |
| >50 – 60                |                 | 10 (6.8)       |
| >60                     |                 | 5 (3.4)        |
| **Nutritional status (by weight for age)** |  |                |
| Underweight (<25th %tile) | 8 (16.0)   | 49 (33.1)      |
| Normal (25th – 75th %tile) | 31 (62.0) | 71 (48.0)      |
| Overweight (>75th – 95th %tile) | 11 (22.0) | 26 (17.6)      |
| Obese (>95th %tile)     | 0               | 2 (1.4)        |

Table 2. Frequency distribution of clinical diagnosis and serotypes of dengue infection among children and adult

| Clinical diagnoses (n = 198) | Children | Adults | Total |
|-----------------------------|----------|--------|-------|
| DF                          | 36/50 (72.0) | 104/148 (70.3) | 140/198 (70.7) |
| DHF grade 1                 | 9/50 (18.0)  | 23/148 (15.5)  | 32/198 (16.2)  |
| DHF grade 2                 | 1/50 (2.0)   | 15/148 (10.1)  | 16/198 (8.1)   |
| DHF grade 3                 | 3/50 (6.0)   | 5/148 (3.4)    | 8/198 (4.0)    |
| DHF grade 4                 | 1/50 (2.0)   | 1/148 (0.7)    | 2/198 (1.0)    |
| **Dengue infection (n = 131)** |     |        |       |
| Primary                     | 1/33 (3.0)   | 3/98 (3.0)     | 4/131 (3.1)    |
| Secondary infection         | 32/33 (97.0) | 95/98 (97.0)   | 127/131 (96.9) |
| **Dengue Serotype (n = 135)** |     |        |       |
| DEN 1                       | 12/34 (35.3) | 18/101 (17.8)  | 30/135 (22.2)  |
| DEN 2                       | 15/34 (44.1) | 51/101 (50.5)  | 66/135 (48.9)  |
| DEN 3                       | 6/34 (17.6)  | 26/101 (25.7)  | 32/135 (23.7)  |
| DEN 4                       | 1/34 (2.9)   | 6/101 (5.9)    | 7/135 (5.2)    |
Table 3. Signs and symptoms in each age group

| Signs/symptoms [n(%)]     | Children (n = 50) | Adults (n = 148) | Odds ratio (95% CI) | P* |
|---------------------------|-------------------|------------------|---------------------|----|
| Headache                  | 47 (94.0)         | 135 (91.2)       | 1.51 (0.41-5.53)    | 0.53 |
| Myalgia/Arthralgia        | 46 (92.0)         | 132 (89.2)       | 1.39 (0.44-4.38)    | 0.57 |
| Retro-orbital pain        | 11 (22.0)         | 56 (37.8)        | 0.46 (0.22-0.98)    | 0.04 |
| Facial flushing           | 12 (24.0)         | 33 (22.3)        | 1.10 (0.52-2.34)    | 0.80 |
| Cough/Runny nose          | 11 (22.0)         | 26 (17.6)        | 1.32 (0.60-2.92)    | 0.49 |
| Abdominal pain            | 16 (32.0)         | 37 (25.0)        | 1.41 (0.70-2.85)    | 0.33 |
| Nausea/Vomiting           | 37 (74.0)         | 113 (76.4)       | 0.88 (0.42-1.84)    | 0.74 |
| Diarrhea                  | 14 (28.0)         | 55 (37.2)        | 0.66 (0.33-1.33)    | 0.24 |
| Hepatomegaly              | 7 (14.0)          | 20 (13.5)        | 1.04 (0.41-2.63)    | 0.93 |
| Splenomegaly              | 1 (2.0)           | 0                | 4.02 (3.15-5.13)    | 0.09 |
| Lymphadenopathy           | 2 (4.0)           | 1 (0.7)          | 6.13 (0.54-69.05)   | 0.10 |
| Rash (fever phase)        | 3 (6.0)           | 2 (1.4)          | 4.66 (0.76-28.73)   | 0.07 |
| Convalescent Rash         | 20 (40.0)         | 46 (31.1)        | 1.48 (0.76-2.87)    | 0.25 |
| Shock                     | 4 (8.0)           | 6 (4.1)          | 2.06 (0.56-7.61)    | 0.27 |

Spontaneous bleeding

| Signs/symptoms [n(%)]     | Children (n = 50) | Adults (n = 148) | Odds ratio (95% CI) | P* |
|---------------------------|-------------------|------------------|---------------------|----|
| Petechiae                 | 6 (12.0)          | 34 (23.0)        | 0.46 (0.18-1.17)    | 0.10 |
| Purpura                   | 1 (2.0)           | 1 (0.7)          | 3.00 (0.18-48.87)   | 0.42 |
| Epistaxis                 | 8 (16.0)          | 10 (6.8)         | 2.63 (0.98-7.09)    | 0.05 |
| Gum bleeding              | 4 (8.0)           | 22 (14.9)        | 0.50 (0.16-1.52)    | 0.21 |
| Melena                    | 0                 | 1 (0.7)          | 1.34 (1.24-14.45)   | 0.56 |
| Hematemesis               | 2 (4.0)           | 1 (0.7)          | 6.13 (0.54-69.05)   | 0.10 |
| Hematuria                 | 1 (2.0)           | 1 (0.7)          | 3.00 (0.18-48.87)   | 0.42 |
| Hypermennorhea*           | 7 (22)            | 22 (70)          | 4.20 (1.28-13.80)   | 0.01 |

*P-value were calculated using Chi square or Fisher-exact tests, * for female aged >10 years

Table 4. Clinical diagnosis of dengue serotype

| Clinical diagnoses [n(%)] | DEN 1 (n = 30) | DEN 2 (n = 66) | DEN 3 (n = 32) | DEN 4 (n = 7) |
|--------------------------|----------------|----------------|----------------|---------------|
| DF                       | 22 (73.3)      | 42 (63.6)      | 22 (68.8)      | 5 (71.4)      |
| DHF                      | 8 (26.7)       | 24 (36.4)      | 10 (31.2)      | 2 (28.6)      |
| DHF grade 1              | 4 (13.3)       | 11 (16.7)      | 6 (18.8)       | 1 (14.3)      |
| DHF grade 2              | 1 (3.3)        | 9 (13.6)       | 3 (9.4)        | 1 (14.3)      |
| DHF grade 3              | 2 (6.7)        | 3 (4.5)        | 1 (3.1)        | 0             |
| DHF grade 4              | 1 (3.3)        | 1 (1.5)        | 0              | 0             |

Table 5. Dengue clinical manifestations by dengue serotype

| Signs/symptoms [n(%)]     | DEN 1 (n = 30) | DEN 2 (n = 66) | DEN 3 (n = 32) | DEN 4 (n = 7) | Total (n = 135) |
|---------------------------|----------------|----------------|----------------|---------------|-----------------|
| Headache                  | 28 (93.3)      | 61 (92.4)      | 30 (93.8)      | 7 (100)       | 126 (93.3)      |
| Myalgia/Arthralgia        | 28 (93.3)      | 58 (87.9)      | 29 (90.6)      | 7 (100)       | 122 (90.4)      |
| Retro-orbital pain        | 12 (40.0)      | 24 (36.4)      | 12 (37.5)      | 6 (85.7)      | 54 (40.0)       |
| Facial flushing           | 9 (30.0)       | 22 (33.3)      | 11 (34.4)      | 3 (42.9)      | 45 (33.3)       |
| Cough/Runny nose          | 3 (10.0)       | 6 (9.1)        | 4 (12.5)       | 0             | 13 (9.6)        |
| Abdominal pain            | 9 (30.0)       | 23 (34.8)      | 8 (25.0)       | 0             | 40 (29.6)       |
| Nausea/Vomiting           | 26 (86.7)      | 48 (72.7)      | 28 (87.5)      | 6 (85.7)      | 108 (80.0)      |
| Diarrhea                  | 9 (30.0)       | 25 (37.9)      | 16 (50.0)      | 3 (42.9)      | 53 (39.3)       |
| Hepatomegaly              | 5 (16.7)       | 11 (16.7)      | 1 (3.1)        | 0             | 17 (12.6)       |
| Lymphadenopathy           | 0              | 2 (3.0)        | 0              | 0             | 2 (1.5)         |
| Rash (fever phase)        | 0              | 2 (3.0)        | 0              | 0             | 2 (1.5)         |
| Convalescent Rash         | 12 (40.0)      | 27 (40.9)      | 15 (46.9)      | 0             | 54 (40.0)       |
| Shock                     | 3 (10.0)       | 4 (6.1)        | 1 (3.1)        | 0             | 8 (5.9)         |
| Signs/symptoms | DEN 1 (n = 30) | DEN 2 (n = 66) | DEN 3 (n = 32) | DEN 4 (n = 7) | Total (n = 135) |
|----------------|----------------|----------------|----------------|--------------|----------------|
| Spontaneous bleeding |                |                |                |              |                |
| Petechiae       | 3 (10.0)       | 9 (13.6)       | 5 (15.6)       | 2 (28.6)     | 19 (14.1)      |
| Purpura         | 0              | 1 (1.5)        | 0              | 0            | 1 (0.7)        |
| Epistaxis       | 4 (13.3)       | 6 (9.1)        | 2 (6.3)        | 0            | 12 (8.9)       |
| Gum bleeding    | 4 (13.3)       | 10 (15.2)      | 5 (15.6)       | 0            | 19 (14.1)      |
| Melena          | 0              | 1 (1.5)        | 0              | 0            | 1 (0.7)        |
| Hematemesis     | 1 (3.3)        | 1 (1.5)        | 1 (3.1)        | 0            | 3 (2.2)        |
| Hypermenorrhea* | 4/9 (44.4)     | 4/34 (11.8)    | 4/18 (22.2)    | 0            | 12 (19.4)      |

Table 6. Clinical manifestations by DEN 2 and non-DEN 2 infection

| Signs/symptoms | DEN 2 (n = 66) | Non-DEN 2 (n = 69) | Odds ratio (95% CI) | P* |
|----------------|----------------|--------------------|---------------------|----|
| Headache       | 61 (92.4)      | 65 (94.2)          | 0.75 (0.19-2.9)     | 0.68 |
| Myalgia/Arthralgia | 58 (87.9) | 64 (92.8) | 0.57 (0.18-1.8) | 0.34 |
| Retro-orbital pain | 24 (36.4) | 30 (43.5) | 0.74 (0.37-1.48) | 0.40 |
| Facial flushing | 22 (33.3)      | 23 (33.3)         | 1.00 (0.49-2.05)   | 1.00 |
| Cough/Runny nose | 6 (9.1)     | 7 (10.1)          | 0.89 (0.28-2.79)   | 0.84 |
| Abdominal pain  | 23 (34.8)      | 17 (24.6)         | 1.64 (0.78-3.45)   | 1.69 |
| Nausea/Vomiting | 48 (72.7)      | 60 (87.0)         | 0.40 (0.17-0.97)   | 0.04 |
| Diarrhea        | 25 (37.9)      | 28 (40.6)         | 0.89 (0.45-1.78)   | 0.75 |
| Hepatomegaly    | 11 (16.7)      | 6 (8.7)           | 2.10 (0.73-6.05)   | 0.16 |
| Lymphadenopathy | 2 (3.0)        | 0                 | n/a                | 0.24 |
| Rash (fever phase) | 2 (3.0)  | 0                 | n/a                | 0.24 |
| Convalescent Rash | 27 (40.9)   | 27 (39.1)        | 1.08 (0.54-2.15)   | 0.83 |
| Shock           | 4 (6.1)        | 4 (5.8)           | 1.05 (0.25-4.38)   | 0.95 |
| Spontaneous bleeding |          |                |                    |    |
| Petechiae       | 9 (13.6)       | 10 (14.5)         | 0.93 (0.35-2.46)    | 0.89 |
| Purpura         | 1 (1.5)        | 0                 | n/a                | 0.45 |
| Epistaxis       | 6 (9.1)        | 6 (8.7)           | 1.05 (0.32-3.44)   | 0.94 |
| Gum bleeding    | 10 (15.2)      | 9 (13.0)          | 1.19 (0.45-3.15)   | 0.73 |
| Melena          | 1 (1.5)        | 0                 | n/a                | 0.49 |
| Hematemesis     | 1 (1.5)        | 2 (2.9)           | 0.52 (0.05-5.82)   | 1.00 |
| Hypermenorrhea* | 4/34 (11.8)    | 8/28 (28.6)       | 0.33 (0.09-1.26)   | 0.12 |

* P-value were calculated using Chi square or Fisher-exact tests
b for female aged >10 years
n/a = not applicable

Due to most prevalence of DEN2 in this study, further analysis between DEN2 and non-DEN2 was done. We correlated clinical manifestations by DEN 2 and non-DEN 2. We found that nausea/vomiting was more common in non-DEN2 than DEN2 infection (87.0% vs 72.7%) (Table 6).

4. DISCUSSION

In this study, the most prevalent age group was >18-30 years, followed by >9-18 years. This result was compatible with data from Thai Bureau of Epidemiology in 2013 showing that most cases of DF and DHF in Thailand were in age 15-24 years, followed by 10-14 years with the ratio of DF: DHF of 56.6%; 43.4% [20]. The difference of national proportion of DF: DHF from our study may be from our institute's policy to early admit cases with dengue infection, therefore, DF cases were around 70% of total cases. Our results were the same as a previous study about annual incidence rate in South China during 2005 - 2011 showing that adults 20-39 years of age had the highest incidence and the vast majority of cases presented with a mild manifestation typical to dengue fever [21]. The findings from India about the changing epidemiology of dengue showed that the most predominant age group was between 21 – 30 years and it was similar to our study [5,22]. Moreover studies in Brazil and Taiwan also
proved the same [23,24]. In contrary to other study, DHF have more prevalent in admitted cases than DF in children population between 2-15 years [25]. Most of our subjects were older children and adults. As a result, most subjects in our study were secondarily infected (96.9%) which was similar to previous study conducted in Chonburi [26]. About 3% of adults in this study were primary infection (two DF, one DHF), which was the same as previous study [27,26]. We could not demonstrate dengue severity related to nutritional status because only 2 obese adults were found in our study (1 DF and 1 DHF). No death was found in our study.

Dengue serotype prevalence in our study were consistent with national dengue in Thailand in 2011 - 2012 showing that serotype 2 was the most prevalent followed by DEN 1 and DEN 3. When compared to data in 1994 to 2006 in Bangkok, DEN 1 (36%) was the most prevalent serotype, followed by DEN 2 (23%), and DEN 3 (27%), but there was no significant rate of DHF by serotype [28]. One of the study from outside of Bangkok in 2002 mentioned that DEN 2 was most frequent (54.5%) followed by DEN 1 (21.2%), DEN 3 (12.1%) and DEN 4 (12.1%) [29]. These finding showed that 4 dengue serotypes had been circulating in Thailand. DENV 2 (57.1 %) was reported to be most common in Singapore followed by DENV 1 (22 %), DENV 3 (17.1 %) and DENV 4 (3.8 %) [30]. In Taiwan and Caribbean island, Sint Eustatius, DENV 2 was the most dominant serotype [31,32]. Studies from Malaysia showed that DENV 1 (25.53 %) was most prevalent followed by DENV 3 (23.40 %), DENV 4 (12.77%) and DENV 2 (10.64%) [33].

We found that adults in our study had more retro-orbital pain, nausea and arthralgia than children. The spontaneous bleeding was more common in children than adults. With more details, children had more epistaxis and hypermenorrhea while adults had gum bleeding and petechiae. Some data reported that children tended to have more cough, vomiting, abdominal pain, rash (including convalescent rash), disturbance of consciousness and epistaxis than adults, while adults had more myalgia and gum bleeding [34,35].

Regarding dengue serotypes, we found subjects with DEN 1 tended to have more mucosal bleeding including epistaxis and hypermenorrhea, whereas Limkittikul reported that rate of bleeding manifestation was less likely found in DEN 1(7.6%) vs (25%, 37%, 42.8%) in DEN 2, DEN 3 and DEN 4 respectively. We also found more shock in DEN 1and DEN 2 infection, which was similar to previous study showing that 2 common dengue serotypes with shock were DEN 2 followed by DEN 1 [31]. Another study also reported that subjects infected with DEN 2 had significantly more shock and internal bleeding, whereas plasma leakage was more common in DEN1 [36]. Laboratory parameters in our study showed that lowest of WBC, highest AST and ALT were found in non-DEN 2. Previous study found that lowest level of WBC found in DEN 1, while the highest was in DEN 3 [31].

Hospital based study from India showed that among 4 serotypes, only abdominal pain and hepatomegaly were significantly different and most predominant in DEN 2, which had the same trend in this study [37]. Limkittikul showed the ratio of DF/DHF in DEN 2 was lowest among 4 serotypes indicating more severe of clinical diagnosis on DEN 2 [29].

In a study in Nicaragua compared clinical manifestations among infants, children and adult. Shock, plasma leakage and marked thrombocytopenia were found more in younger age especially infants and 5 to 7 years old. Epistaxis, hypotension and anorexia were found more in children [38]. However, this study could not demonstrate this finding due to less number of younger children.

There were 10 subjects with dengue shock syndrome in our study. Nine of them resulted from secondary dengue infection, which may reflect the hypothesis of enhancing antibody. However, there was one exceptional case with primary infection.

5. CONCLUSION

We found around 70% of cases in the study diagnosed as DF in both children and adults. Most of the cases were secondary dengue infection. Typical symptoms in adult involved retro orbital pain, nausea and arthralgia while children might suffer epistaxis and hypermenorrhea. The most prevalent dengue serotype in our study was serotype 2. We found that DEN 1 tended to have more mucosa bleeding and shock. In DEN 4 infection, subjects had more retro-orbital pain and skin bleeding.
COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Henchal EA, Putnak JR. The dengue viruses. Clin. Microbiol. Rev. 1990;3(4):376–96.
2. Gubler DJ. Dengue and dengue hemorrhagic fever. Clin. Microbiol Rev. 1998;11(3):480–96.
3. Simmons CP, Farrar JJ, Nguyen V, Wills B, et al. Dengue. N Eng J Med. 2012;366(15):1423–32.
4. Gould EA, Solomon T. Pathogenic flaviviruses. Lancet. 2008;371(9611):500-9.
5. Gubler DJ. Dengue and Dengue Hemorrhagic Fever: Its History and Resurgence as a Global Public Health Problem. In: Gubler DJ, Kuno G, eds. Dengue and Dengue Hemorrhagic Fever. London: CAB International. 1997:1–22.
6. Ferreira GL. Global dengue epidemiology trends. Rev Inst Med Trop Sao Paulo. 2012 October 54 (Suppl 18); SS–S6.
7. Duyen HT, Ngoc TV, Ha do T, Hang VT, Kieu NT, Young PR, et al. Kinetics of plasma viremia and soluble nonstructural protein 1 concentrations in dengue: differential effects according to serotype and immune status. J Infect Dis. 2011;203:1292–1300.
8. Rigau-Perez J. Severe dengue: the need for new case definitions. Lancet Inf Dis. 2006;6:297-302.
9. Guzman MG, Kouri GP, Bravo J, Soler M, Vazquez S, et al. Dengue hemorrhagic fever in Cuba, 1981: A retrospective seroepidemiologic study. Am J Trop Med Hyg. 1990;42:179-84.
10. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: WHO; 2009.
11. Gulati S, Maheshwari A. Atypical manifestations of dengue. Trop Med Int Health. 2007;12:1087-95.
12. Solomon T. Viral encephalitis in Southeast Asia. Neurological Infections and Epidemiology. 1997;2:191-9.
13. Kalayanarooj S, Changsiriwongs V, Nimmannitya S. Dengue patients at the Children's Hospital, Bangkok: 1995-1999 review. Dengue Bulletin. 2002;26:33-43.
14. Cam BV, Fonsmark L, Hue NB, Phuong NT, Poulsen A, Heegaard ED. Prospective case-control study of encephalopathy in children with dengue haemorrhagic fever. Am J Trop Med Hyg. 2001;65:848-51.
15. Lum CS, Thong MK, Cheah YK, Lam SK. Dengue-associated adult respiratory distress syndrome. Ann Trop Paediatr. 1995;15:335-9.
16. Pal S, Dauner AL, Mitra I, Forshey BM, Garcia P, et al. Evaluation of dengue NS1 antigen rapid test and ELISA kits using clinical samples. Plos Negl Trop Dis. 2014;9:e113411.
17. Shu PY, Huang JH. Current advances in dengue diagnosis. Clin Diagn Lab Immunol. 2004;11:642–650.
18. Lanciotti RS, Calisher CH, Gubler DJ, Chang GS, Vromdam AV. Rapid detection and typing of dengue viruses from clinical specimens by using transcriptase-polymerase chain reaction. J Clin Microbiol. 1992;30:545-551.
19. Libraty DH, Young PR, Pickering D, Endy TP, Kalayanarooj S, Green S, et al. High circulating levels of the dengue virus nonstructural protein NS1 early in dengue illness correlate with the development of dengue hemorrhagic fever. J Infect Dis. 2002;186:1165–1168.
20. Thai Bureau of epidemiology. Annual report [online]; 2012. Available: http://www.boe.moph.go.th/AnnualReport/index.html
21. Guo R, Lin J, Li L, Ke C, He J, Zhong H, et al. The prevalence and epidemic nature of dengue infections in Guangdong, South China: An epidemiological, sererological and etiological study from 2005-2011. Plos Negl Trop Dis. 2014;8:e85596.
22. Gupta E, Dar L, Kapoor G, Broor S. The changing epidemiology of dengue in Delhi, India. Virology Journal. 2006;3:92.
23. Chu YW, Tung VVN, Cheung TKM, Chu MY, Cheng N, Lai C, et al. Change in age pattern of persons with dengue, Northern Brazil. Emerg Infect Dis. 2011;17:132–133.
24. Yamamoto Y, Takasaki T, Yamada K, Kimura M, Washizaki K, et al. Acute disseminated encephalomyelitis following dengue fever. J Inf Chemother. 2002;8:175-7.
25. Panpitpat C, Panpitpat A, Hemungkorn M. Dengue patients in different age groups. Asian-Oceanian J Pediatr Child Health. 2007;6:1-7.
26. Wichmann O, Hongsiriwon S, Bowonwatanuwanong C, Chotivanich K, Sukthana Y, Pukrittayakamee S. Risk factors and clinical features associated with severe dengue infection in adults and children during the 2001 epidemic in Chonburi, Thailand. Trop Med Int Health. 2004;9:1022–9.
27. Kittigul L, Pitakarnjanakul P, Sujirarat D, Siripanichgon K. The differences of clinical manifestations and laboratory findings in children and adults with dengue virus infection. J Clin Virol. 2007;39:76–81.
28. Fried JR, Gibson RB, Kalayanarooj S, Thomas SJ, Srikiatkhachorn A, Yoon IK, et al. Serotype-specific differences in the risk of dengue hemorrhagic fever: An analysis of data collected in Bangkok, Thailand from 1994 to 2006. Plos Negl Trop Dis. 2010;4(3):e617.
29. Limkittikul K, Yingsakmongkon S, Jittmittraphap A, Chuananon S, Kowasupathr S, et al. Clinical difference among PCR-proven dengue serotype infections. Southeast Asian J Trop Med Public Health. 2005;36:1432-8.
30. Yung CF, Lee KS, Thein TL, Tan LK, Gan VC, et al. Dengue serotype-specific differences in clinical manifestation, laboratory parameters and risk of severe diseases in adults, Singapore. Am J Trop Med Hyg. 2015;92(5):999-1005.
31. Leslie T, Martin NJ, Roosberg CJ, Odongo G, Beausoleil E, et al. Dengue serosurvey in Sint Eustatius. Plos Negl Trop Dis. 2014;9(6):e95002.
32. Wang CC, Lee IK, Su MC, Lin HI, Huang YC, et al. Differences in clinical and laboratory characteristics and disease severity between children and adults with dengue virus infection in Taiwan, 2002. Trans R Soc Trop Med Hyg. 2009;103: 871-877.
33. Ab-Fatah M, Subenthiran S, Abdul-Rahman PSA, Saat Z, Thayan R. Dengue serotype surveillance among patients admitted for dengue in two major hospitals in Selangor, Malaysia, 2010-2011. Tropical Biomedicine. 2015;32(1):187-191.
34. Hanafusa S, Chanyasanha C, Sujirarat D, Khuankhunsathid I, Yaguchi A,Suzuki T. Clinical features and difference between child and adult dengue infections in rayong province, southeast Thailand. Southeast Asian J Trop Med. 2008;39:252-60.
35. Souza LJ, Pessanha LB, Mansur L, Souza LA de, Ribeiro MBT, Silveira MV, et al. Comparison of clinical and laboratory characteristics between children and adult with dengue. Bra J Inf Dis. 2013;17:27-31.
36. Balmaseda A, Hammond SN, Perez L, Tellez Y, Saborio SI, Mercado JC, et al. Serotype-specific differences in clinical manifestations of dengue. Am J Trop Med Hyg. 2006;74(3):449-56.
37. Kumaria R. Correlation of disease spectrum among four Dengue serotypes: a five years hospital based study from India. Braz J Infect Dis. 2010;14(2):141- 6.
38. Hammond NS, Balmaseda A, Perez L, Tellez Y, Saborio SI, Mercado JC, et al. Difference in dengue severity in infant, children and adult in a 3 years hospital-based study in Nicaragua. Am J Trop Med Hyg. 2005;73:1063–70.