MANIFESTATIONS OF DENGUE IN VARIOUS AGE GROUPS OF THAI CHILDREN AND ADULTS: A CROSS SECTIONAL STUDY

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Abstract. Dengue is the most common mosquito-borne virus causing disease in many countries. The disease, caused by dengue serotypes 1 to 4, ranges from asymptomatic infection, undifferentiated fever, dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). Early recognition of the disease is one of the key factors for successful treatment, and is only possible if the diagnostician knows the patient-specific clinical manifestations. We studied the clinical manifestations in dengue patients to determine the most common manifestations of dengue infection by age group. Clinical data of dengue patients admitted to Photharam Hospital, Ratchaburi, Thailand during 2005-2015 were analyzed. The patients were classified into eight different age groups: 0-1 years, 2-5 years, 6-9 years, 10-14 years, 15-18 years, 19-29 years, 30-59 years, and ≥60 years. For all age groups, fever, anorexia, nausea, and vomiting were most common. However, seizures and diarrhea were more common in children aged <1 year. In regards to dengue severity, DHF was more common in older children and young adults while DF was more common in younger children and ageing adults. Our study emphasizes the significant variance of clinical manifestations in different age groups, suggesting that proper management must consider the different age-specific clinical manifestations.

Keywords: dengue, manifestations, age groups, children, adults

INTRODUCTION

Dengue infection, a mosquito-borne viral disease of humans, is now a significant problem in many countries. It can present itself in many forms, ranging from asymptomatic infection, undifferentiated fever, dengue fever (DF) to severe dengue hemorrhagic fever (DHF) with or without shock. DHF is characterized by fever, bleeding diathesis, and the possibility of developing a potentially fatal shock syndrome. The most common hematological findings include vasculopathy, coagulopathy, and thrombocytopenia (Thisyakorn and Thisyakorn, 2015a). In 2009, the World Health Organization has developed a severity-based revised dengue classification for medical interventions, which has been used in most countries (WHO, 2009).

Laboratory diagnosis includes virus isolation, serology, and detection of dengue ribonucleic acid. Successful treatment depends on early recognition of the disease and careful monitoring for shock. There are currently no licensed antivirals to treat dengue. The use of safe and efficacious dengue vaccine along with vector control innovations will lead to successful prevention and control of dengue (Thisyakorn and Thisyakorn, 2015a).

In the past decades, a trend of increasing age in dengue patients has been evidented. Moreover, clinical presentations and laboratory findings of dengue infections may be different in each age group (Kittigul *et al,* 2007; de Souza *et al,* 2013; Tantawichien, 2015). Thus, this study analyzes the magnitude of clinical manifestation variation among dengue patients of different ages.

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MATERIALS AND METHODS

Study design

This descriptive study was conducted in Photharam Hospital, Ratchaburi, Thailand during 2005- 2015.

Study subjects

The medical charts of all hospitalized patients with dengue infection were reviewed. Dengue patients were divided into eight different age groups: 0-1 years, 2-5 years, 6-9 years, 10-14 years, 15-18 years, 19-29 years, 30-59 years, and ≥60 years. Diagnosis of dengue infection adhered to clinical and laboratory criteria for the diagnosis of DHF as established by the World Health Organization (WHO, 1997) as follows:

Clinical criteria:

1. Acute fever: high, continuous, lasting for 2-7 days.
2. Hemorrhagic manifestations such as a positive tourniquet test, petechiae, purpura, ecchymosis, epistaxis, bleeding gums, hematemesis, or melena.
3. Hepatomegaly.
4. Shock – a rapid, weak pulse with a narrow pulse pressure; hypotension with cold, clammy skin, and restlessness.

Laboratory criteria:

1. Thrombocytopenia (platelet count < 100,000/mm^3).
2. Hemoconcentration (hematocrit increased from baseline by > 20%).

In patients with DHF grade I, a positive tourniquet test is the only hemorrhagic manifestation whereas in DHF grade II spontaneous bleeding occurs. Patients with circulatory failure (a narrowing of the pulse pressure and a rapid and weak pulse) have DHF grade III. Patients in profound shock (no detectable blood pressure and pulse) have DHF Grade IV. DHF III and IV are also referred to as DSS.

Data collection and analysis

Data obtained from the medical records were age, sex, date of hospitalization, severity of disease, clinical manifestations, laboratory findings, complications, and outcome. Descriptive data were analyzed using mean, range, and percentage. Variables were compared using chi-square test.

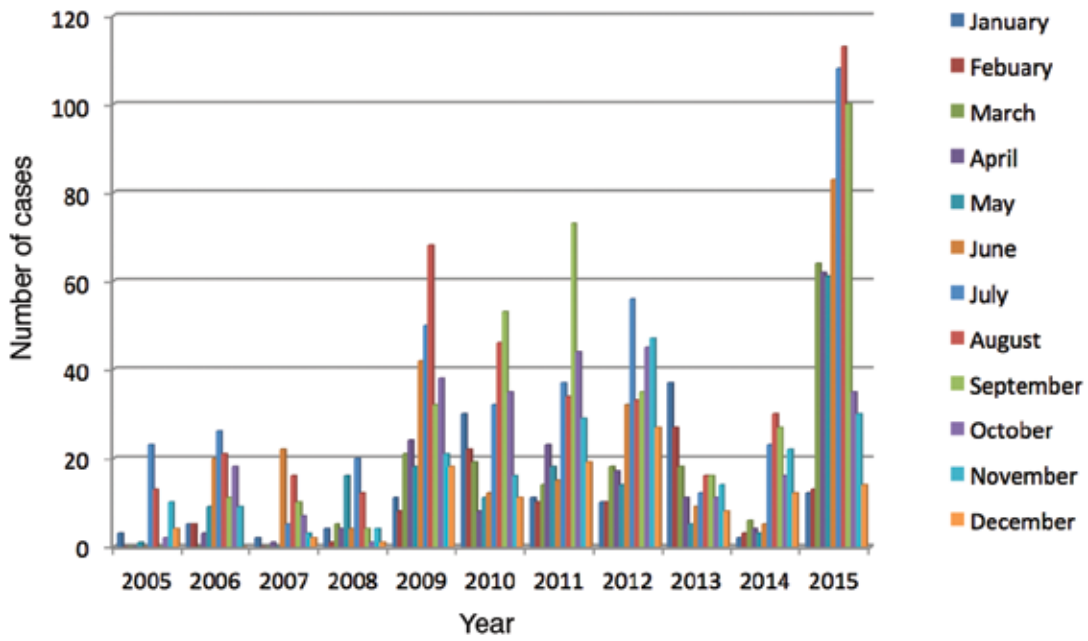

Fig 1–Seasonal distribution of dengue patients in Photharam Hospital, Ratchaburi, Thailand between 2005 and 2015.

The level of significance was set at p-value <0.05.

RESULTS

During the period of study, we analyzed 2,676 cases, of which there were 37 cases in the 0-1 year age group (1.38%), 156 cases in the 2-5 years age group (5.83%), 375 cases in the 6-9 years age group (14.01%), 622 cases in the 10-14 years age group (23.24%), 406 cases in the 15-18 years age group (15.17%), 614 cases in the 19-29 years age group (22.95%), 435 cases in the 30-59 years age group (16.26%), and 31 cases in ≥60 years age group (1.16%).

The gender composition comprised of 1,297 males and 1,379 females. The disease was seen all year round with higher incidence in the rainy season, which begins in June and usually lasts until October (Fig 1). Fig 2 shows the age distribution of dengue patients during the study period.

The most common symptoms across age groups were fever, anorexia, nausea, and vomiting. Respiratory symptoms, diarrhea, and seizures were more common in children aged <1 year (p<0.05). However, older children and adults presented more commonly with headache and myalgia. Gastrointestinal bleeding and hypermenorrhea were more common in older children and adults (Table 1).

Complete blood counts in teenagers and adults showed that the maximal hematocrit (Hct) was significantly higher whereas the minimal white blood cell (WBC) count was significantly lower. In contrast, the maximal Hct in infants was significantly lower whereas the WBC count was significantly higher (Table 2).

Patients were diagnosed with either dengue DF, DHF, or DSS. All severities of dengue diseases were seen in all age groups (Fig 3). The overall mortality rate was 0.11%.

DISCUSSION

Our study showed that several manifestations of dengue patients in young children are prominent. They presented significantly more frequently with upper respiratory symptoms and convulsion than the older age groups. Skin bleeding was also more pronounced than bleeding of the mucous membrane or gastrointestinal tract in the infant group.

In the older age groups, we detected five leading manifestations including fever, vomiting, anorexia, abdominal pain, and headache, all

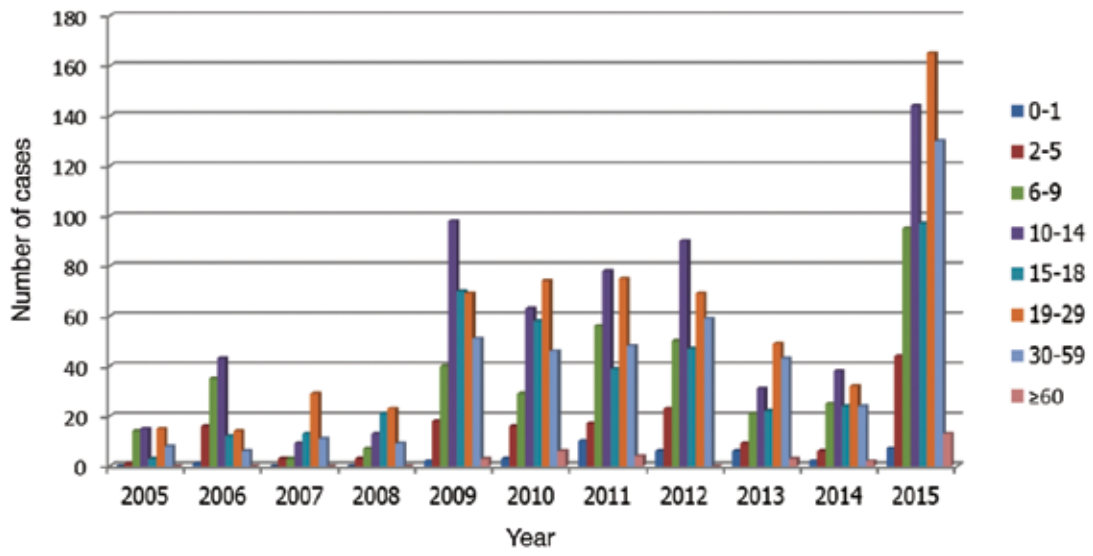

Fig 2–Age distribution of dengue patients in Photharam Hospital, Ratchaburi, Thailand between 2005 and 2015.

Table 1. Clinical manifestations of dengue patients in Photharam Hospital, Ratchaburi, Thailand between 2005 and 2015.

Clinical manifestations	0-1 yrs (*n*=37) *n* (%)	2-5 yrs (*n*=156) *n* (%)	6-9 yrs (*n*=375) *n* (%)	10-14 yrs (*n*=622) *n* (%)	15-18 yrs (*n*=406) *n* (%)	19-29 yrs (*n*=614) *n* (%)	30-59 yrs (*n*=435) *n* (%)	≥60 yrs (*n*=31) *n* (%)
Headache	1 (2.70)	31 (19.87)	152 (40.53)	316 (50.80)	239 (58.87)	368 (59.93)	258 (59.31)	12 (38.71)
Respiratory symptoms	23 (62.16)	69 (44.23)	160 (42.67)	215 (34.57)	124 (30.54)	156 (25.41)	103 (23.68)	10 (32.26)
Anorexia	14 (37.84)	76 (48.72)	208 (55.47)	325 (52.25)	176 (43.35)	244 (39.74)	168 (38.62)	11 (35.48)
Nausea	6 (16.22)	61 (39.10)	16 (4.27)	291 (46.78)	230 (56.65)	355 (57.82)	262 (60.23)	14 (45.16)
Vomiting	15 (40.54)	80 (51.28)	198 (52.80)	329 (52.89)	203 (50.00)	303 (49.35)	211 (48.51)	11 (35.48)
Abdominal pain	1 (2.70)	33 (21.15)	125 (33.33)	191 (30.71)	113 (27.83)	174 (28.34)	121 (27.82)	7 (22.58)
Diarrhea	14 (37.84)	24 (15.38)	49 (13.07)	95 (15.27)	67 (16.50)	77 (12.54)	45 (10.34)	1 (3.23)
Seizures	6 (16.22)	2 (1.28)	1 (0.27)	6 (0.96)	1 (0.25)	1 (0.16)	1 (0.23)	0 (0.00)
Hepatomegaly	2 (5.41)	9 (5.77)	29 (7.73)	43 (6.91)	8 (1.97)	18 (2.93)	5 (1.15)	0 (0.00)
Splenomegaly	0 (0.00)	1 (0.64)	1 (0.27)	2 (0.32)	2 (0.49)	1 (0.16)	0 (0.00)	0 (0.00)
				Site of bleeding				
Skin	2 (5.41)	1 (0.64)	1 (0.27)	2 (0.32)	4 (0.99)	5 (0.81)	17 (3.91)	1 (3.23)
Gastrointestinal tract	0 (0.00	3 (1.92)	5 (1.33)	25 (4.02)	7 (1.72)	16 (2.61)	12 (2.76)	0 (0.00)
Mucous membrane	0 (0.00)	13 (8.33)	43 (11.47)	70 (11.25)	23 (5.67)	47 (7.65)	27 (6.21)	2 (6.45)
Hypermenorrhea	0 (0.00)	0 (0.00)	0 (0.00)	36 (5.79)	1 (0.25)	59 (9.61)	32 (7.36)	0 (0.00)

Table 2. Mean values of complete blood count of dengue patients in Photharam Hospital, Ratchaburi, Thailand between 2005 and 2015.

Complete blood count	0-1 yrs *n*=37	2-5 yrs *n*=156	6-9 yrs *n*=375	10-14 yrs *n*=622	15-18 yrs *n*=406	19-29 yrs *n*=614	30-59 yrs *n*=435)	≥60 yrs *n*=31
Hct max (%)	35.75	37.99	39.39	42.17	43.14	43.09	42.13	39.8
Hct min (%)	31.56	34.14	36.76	37.77	38.23	38.29	37.57	35.78
WBC min (/mm^3)	6,828.65	3,896.36	3,237.85	2,717.59	2,795.61	3,392.76	3,595.05	3,180.65
Plt min (/mm^3)	61,351.35	88,802.55	85,781.79	75,469.00	64,126.23	57,984.08	60,701.23	67,645.16

Hct, hematocst; WBC, white blood cell; Plt, plateless.

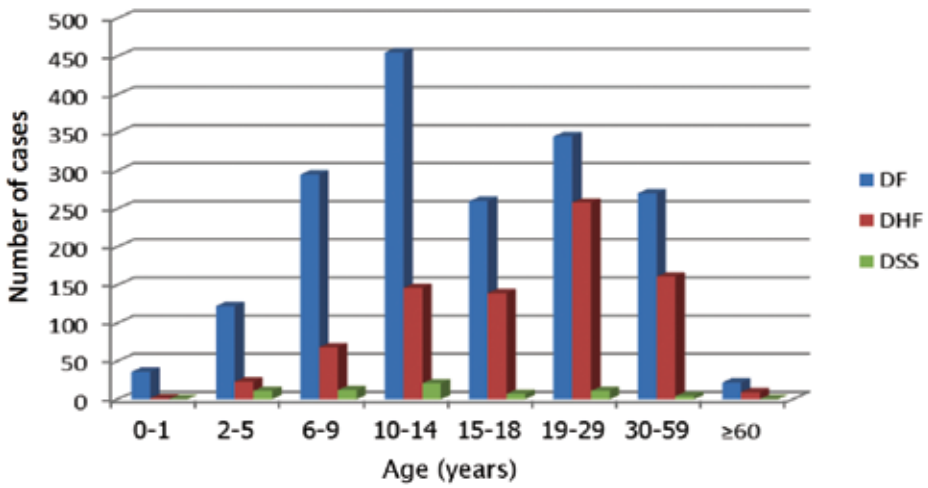

Fig 3–Severity of dengue patients by age group in Photharam Hospital, Ratchaburi, Thailand between 2005 and 2015.

of which are in agreement with those from a previous report that identified the same leading manifestations (Tantawichien, 2015). The older age groups may have more commonly self-reported headache, abdominal pain, and myalgia than children because the older age groups may have been better able to explain their symptoms than young children.

Hypermenorrhea with clinical significance was seen in older girls and young women with dengue infections. The menstrual period was essential in all girls and women who presented with clinical manifestations compatible with dengue infections since hormonal therapy to stop the bleeding may be necessary.

Normal infants tend to have a higher WBC count as their baseline levels whereas older children and adults tend to have higher Hct level and a lower WBC count (Walters and Abelson, 1996). In our study, this may explain why infants with dengue infection had higher profiles on WBC count in comparison to the other age groups, and also why dengue-infected teenagers and adults had significantly higher average values of Hct and lower average values of WBC count. Moreover, the severity of plasma leakage may be higher in older children, resulting in higher Hct levels observed in our study.

A previous study on the dynamics of WBCs in dengue patients demonstrated that the number

and types of WBCs changed dynamically with dates of illnesses (Wells *et al,* 1980). Studying the dynamics of these cells in different age groups of dengue-infected children may help to explain the difference in complete blood counts between different age groups.

Our study showed that all severities of dengue diseases could be seen in all age groups. In infants, the diagnostician should not exclude the possibilities of dengue in the infant who presents with high fever, respiratory problems, and central nervous system manifestations. Those central nervous system manifestations are possibly due to febrile convulsions, encephalopathy, and dengue encephalitis (Thisyakorn and Thisyakorn, 2015b).

Early recognition of dengue patients is essential to arrive at an accurate diagnosis and provide prompt treatment. This study emphasizes the prominently different ways that dengue infections can manifest in different age groups, and also shows that age is probably a major determinant of the clinical manifestations that are most likely in a dengue-infected patient.

In condusion, dengue is one disease entity with different clinical manifestations often with unpredictable clinical outcomes. Successful treatment, which is mainly symptomatic and supportive, depends on the early recognition of the disease and careful monitoring of the disease severity. Proper management must consider the different age-specific clinical manifestations.

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