CLINICAL FEATURES AND DIFFERENCES BETWEEN CHILD AND ADULT DENGUE INFECTIONS IN RAYONG PROVINCE, SOUTHEAST THAILAND

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Abstract. A retrospective study was conducted among patients with dengue infection admitted to Rayong Hospital during September 2004-September 2005. Data were collected from medical charts and outpatient records created when the patients came to the hospital. Of the patients diagnosed with dengue, only 301 who met the WHO criteria for dengue fever and DHF/DSS were selected. The study cohort was comprised of 147 children (76 males, 71 females) and 154 adults (71 males, 83 females), with an overall mean age of 17.6 years. Some adult clinical symptoms were different from the children. Headache and myalgia were more common among adults ($p<0.05$), but cough, vomiting, abdominal pain, and rash were more common among children ($p<0.05$). Among the major bleeding symptoms, epistaxis (nasal bleeding) was more common in children ($p=0.012$) and gum bleeding was more common in adults ($p<0.001$). Myalgia was more likely in less severe grades of infection. Adults showed some different clinical manifestations of dengue infection from children. It is necessary for health personnel to take these differences into consideration when seeing probable cases of dengue infection.

INTRODUCTION

In recent years, the global prevalence of dengue has grown dramatically, and it is now endemic in >100 countries. Southeast Asia and the Western Pacific are most seriously affected. The World Health Organization estimates about 50 million cases of dengue infection occur worldwide each year. At least 100 countries are endemic for dengue hemorrhagic fever (DHF) and about 40% of the world's population (2.5 billion people) is at risk in the tropics and subtropics (WHO, 2002). In several Asian countries, about 400,000 cases of DHF are reported annually; this infection is a leading cause of childhood mortality (WHO, 2006). Despite measures taken to prevent and control dengue, DHF has been a major public health problem in Thailand over the past 30 years, without a declining trend (Ministry of Public Health, 2001-2004). This study was conducted in Rayong Province, in southeast Thailand, 179 km from Bangkok. With 275.54 reported dengue cases per 100,000 people in 2003, Rayong Province had the highest prevalence in Thailand (Ministry of Public Health, 2003).

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 (Garcia-Rivera and Rigau-Perez, 2003; Witayathawornwong, 2005). Clinical

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manifestations have also become more diversified, and there have been some reports of dengue infection showing unusual clinical manifestations in both pediatric and adult cases (Torres *et al,* 2000; Yamamoto *et al,* 2002b), but little detailed information is available about the differences between the two groups; therefore, it has become increasingly important to elucidate the clinical differences between them.

MATERIALS AND METHODS

A retrospective study was conducted on dengue patients admitted to Rayong Hospital during the period September 2004-September 2005. Rayong Hospital is one of the provincial hospitals in Thailand. Data were collected from medical charts and outpatient records created when the patients came to the hospital. Of the patients diagnosed with dengue infection, only 301 met the WHO criteria for dengue fever or DHF (Grade I, II without shock, DSS with shock) were selected. The cases were divided into two case groups, children <15 years of age, and adults aged ≥15 years. The clinical symptoms and manifestations of these two groups were compared. The WHO criteria were considered acceptable and adequate for endemic situations, such as in this province. The criteria for a diagnosis of DF were: (1) sudden onset of fever for >2 days; (2) the following symptoms: headache, vomiting, abdominal pain, myalgia, arthralgia, and rash; and (3) thrombocytopenia or leukocytopenia. The criteria for a diagnosis of DHF were: (1) fever: acute onset, high and continuous, lasting >2 days; (2) >1 hemorrhagic manifestation; (3) thrombocytopenia (100,000 /mm^3 or less); (4) signs of hemoconcentration and/or plasma leakage, which were defined by (a) a hematocrit ≥20% (≥20% above average for age, sex and population), or (b) drop in hematocrit following volume replacement ≥20% of hematocrit at presentation, (c) signs of plasma leakage evidenced by plural effusion, ascitics, increase in body weight during hospitalization. The WHO criteria for diagnosis of shock were also used to grade dengue infection. Shock status for grading dengue shock syndrome (DSS: DHFIII, IV) was either a pulse pressure ≤20 mmHg or hypotension for age (systolic blood pressure <80 mmHg if <5 years old or 90 mmHg if ≥5 years old). Patients referred to other hospitals post-admission were excluded. Patients with laboratory examinations suggesting an alternative diagnosis (*eg* malaria, leptospirosis, typhoid fever) were also excluded.

Descriptive statistics were used to describe general characteristics, signs and symptoms. The chi-square and Fisher's exact tests were used for categorical variables. Normally distributed continuous variables were compared by unpaired *t*-test. Where the data did not follow normal distribution, Mann-Whitney or Kruskal-Wallis tests were used.

RESULTS

Of the patients admitted to Rayong Hospital with a diagnosis of dengue infection September 2004 - September 2005, 301 were selected for this study (147 children and 154 adults), with an overall mean age of 17.6 years. The children were comprised of 76 males and 71 females, and the adults 71 males and 83 females. The comparative sex distributions of the children and adults were not significantly different (Table 1).

In general, the children had longer periods of fever post-admission than the adults (2.16 days for children; 1.71 days for adults, p=0.007). However, there were no significant differences between the two groups for total febrile period or length of hospital stay. Regarding the physical signs of the children, degree of fever, and heart and respiratory rates on admission, were significantly higher than the adults (p<0.001). The fever peaks for the

Table 1
Gender and age distribution in children and adults.

No. of patients (%)	Children 147 (48.8)	Adults 154 (51.2)	Total 301 (100)
Gender, no. (%)			
Male	76 (51.7)	71 (48.3)	147
Female	71 (46.1)	83 (53.9)	154
Age mean (SD)	9.31 (3.48)	25.47 (10.46)	

Table 2
Physical signs in children and adults.

No. of patients (%)	Children 147 (48.8)	Adults 154 (51.2)	p-value
Length of fever (days), median (range)			
Before admission	4.00 (0-7)	4.00 (0-7)	0.104
After admission	2.00 (0-8)[a]	1.00 (0-10)	0.007
Height of fever (Celsius), median (range)			
On admission	38.20 (36.0-40.6)	38.00 (35.7-40.4)	0.074
Highest during hospitalization	39.00 (37.0-41.0)[a]	38.75 (36.7-40.9)	< 0.001
Heart rate (/min), median (range)			
On admission	98 (68-163)[a]	88 (60-124)	< 0.001
Highest during hospitalization	104 (82-176)[a]	94 (70-124)	< 0.001
Respiratory rate (/min), median (range)			
On admission	28 (20-48)[a]	22 (18-48)	< 0.001
Highest during hospitalization	28 (18-32)[a]	24 (20-32)	< 0.001

[a]The mean is significantly higher than the other group; p<0.05. (Mann-Whitney test)

children during admission were also significantly higher than the adults (Table 2).

Fever was present in all patients; >50% of both children and adults had symptoms of headache and vomiting. Cough, vomiting, and abdominal pain were more common in children (p<0.05), while headache and myalgia were more common in adults (p<0.05). There were significant differences between child and adult cases with these symptoms (p<0.05). Hepatomegaly was observed in >80% of children examined (Table 3).

Of the clinical bleeding symptoms, epistaxis (nasal bleeding) was more common in children (p=0.012) and gum bleeding was more common in adults (p<0.001). Gastrointestinal bleeding was more common in children. However, there were no significant differences. Tourniquet tests were administered to 57 patients (35 children; 22 adults); positive results (85.7% of children; 54.7% of adults) were more likely in the child cases (p=0.009) (Table 3).

The proportion of DHF (I, II) (49%) among the adults was higher than for the children (33%); however, the proportion of DSS (13%) in adults was similar to the children (12%) (Table 4).

In terms of the clinical symptoms for each grade of dengue infection among the children, children with DSS had more headaches (DSS 68.4%, DHF 55.1%, DF 44.3%), gum bleeding

Table 3
Major clinical signs and hemorrhagic symptoms in children and adults.

	Children(147)	Adults(154)	p-value
Symptoms and signs, no. (%)			
Headache	75 (51.0)	103 (66.9)[a]	0.005
Injected pharynx	36 (24.5)	31 (20.1)	0.363
Cough	52 (35.4)[a]	25 (16.2)	< 0.001
Vomiting	107 (72.8)[a]	95 (61.7)	0.040
Abdominal pain	100 (68.0)[a]	58 (37.7)	< 0.001
Myalgia	18 (12.2)	36 (23.4)[a]	0.012
Joint pain	1 (0.68)	3 (1.95)	0.623
Rash (including convalescent rash)	81 (55.1)[a]	38 (24.7)	< 0.001
Disturbance of consciousness	16 (10.9)[a]	2 (1.3)	< 0.001
Hepatomegaly			
No. examined	39	16	
Positive	32 (82.1)	12 (75.0)	0.712
Hemorrhagic manifestations, no. (%)			
Petechiae	53 (36.1)	58 (37.7)	0.773
Gum bleeding	6 (4.1)	24 (15.6)[a]	< 0.001
Nasal bleeding	17 (11.6)[a]	6 (3.9)	0.012
Hemoptysis	3 (2.0)	3 (1.9)	1.000
Hematemesis	18 (12.2)	9 (5.8)	0.052
Melena	13 (8.8)	9 (5.8)	0.312
Tourniquet test			
No. examined	35	22	
Positive no. (%)	30 (85.7)[a]	12 (54.5)	0.009
Urine blood test			
No. examined	112	133	
Positive no. (%)	61 (54.5)	77 (57.9)	0.590

[a]The proportion is significantly higher than the other group; p<0.05. (Chi-square test)

Table 4
Severity of dengue infection in children and adults.

No. of patients (%)	Children 147 (48.8)	Adults 154 (51.2)
Diagnosis		
DF	79 (54)	60 (39)
DHF I, II	49 (33)	76 (49)
DSS (DHFIII, IV)	19 (13)	18 (12)

(DSS 15.8%, DHF 2.0%, DF 2.5%), abdominal pain (DSS 89.5%, DHF 77.6%, DF 57.0%) and disturbance of consciousness (DSS 36.8%, DHF 10.2%, DF 5.1%) than for the other grades of infection. Adults with DSS showed less headache (DSS 55.6%, DHF 67.1%, DF 70.0%) than for the other grades of infection. Myalgia was less common in the severe grades for both groups (Tables 5, 6).

DISCUSSION

Ideally, confirmation of dengue infection is based on laboratory diagnosis, such as paired serum antibodies, virus isolation (Yamada *et al,* 2002a) and PCR (Chan *et al,* 1994; Gubler, 1996). Some previous publications have used these methods (Phuong *et al,* 2004; Wichmann *et al,* 2004). However, unless patients' samples are taken at appropriate times and examined with sophisticated

Table 5
Symptoms in each grade of dengue infection among children.

	DF (79)	DHF I, II (49)	DSS (19)	Total (147)
Symptoms and signs, no. (%)				
Headache	35 (44.3)	27 (55.1)	13 (68.4)	75 (51.0)
Gum bleeding	2 (2.5)	1 (2.0)	3 (15.8)	6 (4.1)
Nasal bleeding	4 (5.1)	11 (22.4)	2 (10.5)	17 (11.6)
Cough	27 (34.2)	18 (36.7)	7 (36.8)	52 (35.4)
Abdominal pain	45 (57.0)	38 (77.6)	17 (89.5)	100 (68.0)
Myalgia	11 (13.9)	6 (12.2)	1 (5.3)	18 (12.2)
Disturbance of consciousness	4 (5.1)	5 (10.2)	7 (36.8)	16 (10.9)

Table 6
Symptoms in each grade of dengue infection among adults.

	DF (60)	DHF I, II (76)	DSS (18)	Total (154)
Symptoms and signs, no. (%)				
Headache	42 (70.0)	51 (67.1)	10 (55.6)	103 (66.9)
Gum bleeding	6 (10.0)	17 (22.4)	1 (5.6)	24 (15.6)
Nasal bleeding	2 (3.3)	4 (5.3)	0 (0.0)	6 (3.9)
Cough	15 (25.0)	6 (7.9)	4 (22.2)	25 (16.2)
Abdominal pain	20 (33.3)	30 (39.5)	8 (44.4)	58 (37.7)
Myalgia	12 (20.0)	21 (27.6)	3 (16.7)	36 (23.4)
Disturbance of consciousness	0 (0.0)	0 (0.0)	2 (11.1)	2 (1.3)

laboratory techniques, accurate diagnosis is somewhat difficult in local settings. In addition, it is not practical for dengue-endemic developing countries to use such methods in all cases, for economic and technical reasons. Instead of these methods, the WHO criteria have been widely used in endemic areas, especially in dengue-endemic developing countries. The WHO criteria are an acceptable and adequate method for diagnosing dengue infections under such situations (WHO, 2006).

In Southeast Asian countries, DHF is a major killer of children. A pattern of annual outbreaks has been attributed to all four dengue serotypes, with an increasing frequency of sequential infections among children (Gubler, 1993). DHF has been described as a disease that almost exclusively affects children age <16 years (WHO, 2002). In particular, severe dengue infection has been most frequently associated with younger age groups. However, recent studies have suggested a shift in the age distribution of dengue infection to older groups (Garcia-Rivera *et al,* 2003; Ministry of Public Health, 2003). The number of pediatric dengue cases admitted to our hospital was similar to the number of adult cases in our study. This result also seems to reflect a shift in the age distribution of dengue infection.

This study showed the number of male cases to be almost the same as female cases, which is similar to previous studies reporting no significant difference in frequency between

males and females (Garcia-Rivera *et al,* 2003; Wichmann *et al,* 2004). Regarding the relationship between gender and severity among children, Nimmannitya (1987a,b) reported that shock and death occurred more frequently in females than in males. Another study showed that even though the rate of hospitalization of males was higher than females, there was no significant difference in death rate (Garcia-Rivera and Rigau-Perez, 2003). Our study did not find a difference between the genders for hospitalization. Since there were no deaths during the period of study, comparative death rates by gender and age group are not discussed here.

All patients presented with fever during illness; fever is an essential criterion for a diagnosis of DF or DHF/DSS. However, 16% of patients did not have fever on admission; the observed reasons were as follows: (1) although these patients had had a high fever, their symptoms were not sufficiently severe to require hospitalization; therefore, patients may not have come to the hospital; (2) some of the patients were referred from other hospitals; these patients stayed or were observed there during the febrile phase. These phenomena can be explained by the nature of DHF/DSS, where the critical stage is reached by the end of the febrile phase or shortly after a rapid drop in temperature, then circulatory disturbance develops (Nimmannitya, 2002).

This study showed a significant difference between children and adults: higher heart rates and respiratory rates were seen in children compared to adults. These differences are due to physiological differences between the two groups. In terms of the clinical symptoms, adults were more likely to present with headache. This result is the same as a previous study conducted in Chonburi Province, Thailand (Wichmann *et al,* 2004). In contrast, cough, vomiting, and abdominal pain were less common among adults. The proportions of these symptoms in children were similar to previous studies (Garcia-Rivera and Rigau-Perez, 2003; Wichmann *et al,* 2004). Convalescent rash with itching was also more common in children than adults. This may be explained by the relative frequency of secondary infections in adults (Cobra *et al,* 1995). In our study, primary rash was observed in few cases, probably because a large percentage of patients were admitted after this manifestation had abated.

The presence or absense of hepatomegaly were not recorded in any of the hospital records, which constitutes a limitation to the current study. Analysis of the available data shows that adults were less likely to have hepatomegaly. This result agrees with previous studies (Garcia-Rivera and Rigau-Perez, 2003; Wichmann *et al,* 2004). In general, hepatic weight declines with age, which might contribute to this difference between the two groups (Garcia-Rivera and Rigau-Perez, 2003).

Like previous publications (Phuong *et al,* 2004; Nimmannitya, 2002), this study found various hemorrhagic symptoms, the most frequent being hematuria, in both adults and children. Garcia-Rivera and Rigau-Perez (2003) reported a similar result, especially among elderly patients. On the other hand, among children, gastrointestinal bleeding in the form of hematemesis and/or melena was the most common severe bleeding symptom (Nimmannitya*,* 2002). This study also found that gastrointestinal-tract bleeding was a common bleeding manifestation, as well as nasal bleeding in children. The most common bleeding symptom in adults was gum bleeding, where the percentage was significantly higher than in children.

The tourniquet test is recommended as a screening test for dengue infection. One study reported positive rates among child cause in 98.1% and 63.3% for DHF and DF, respectively, and concluded that it is helpful to differentiate it from other febrile illnesses, such as chikungunya (Nimmannitya *et al,* 1969). The WHO case definition requires this

bleeding disorder for grade I DHF, however, the validity of the test has been debated in some publications (Wali *et al,* 1999; Kalayanarooj *et al,* 2003a). Wali *et al* (1999) reported that during the an outbreak in northern India in 1996, only 39.1% of DHF patients were positive by tourniquet test. In our study, not all cases were screened by tourniquet test; among the patients who were, 85.1% of children and 54% of adults were positive using this test. There was a significant difference between the two groups. The tourniquet test results may be inadequate for diagnosis, especially in adults.

Petechiae are a common symptom among dengue patients. One publication reported a rate >90% with petechiae in children with DHF (Kalayanarooj *et al,* 2003b). Other studies have found it in 20-70% (Garcia-Rivera and Rigau-Perez, 2003; Wichmann *et al,* 2004). In this study, 50% of dengue cases had petechiae. There was no significant difference between child and adult cases. The presence of petechiae was significantly related to the minimum number of platelets.

Previous studies reported that in dengue (DF) myalgia was more frequent than with other grades of dengue infection. In our study, myalgia was less likely to be seen in severe grades of dengue infection in both groups, which supports a previous study by Nimmannitya (2002). Almost all clinical symptoms, except disturbance of consciousness, could be seen in every grade of dengue infection, therefore, from clinical symptoms, it is not possible to predict severity of infection.

As already described, there were some significant differences in clinical manifestations between children and adults. However, the mechanisms of these differences are still not clear and further studies are needed. This study was a retrospective study of hospital records; and there were therefore several limitations, especially in relation to some clinical signs and tests.

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