

# Dengue Hemorrhagic Fever in Adults, an Emerging Problem in Thailand: a Retrospective Study of 75 Adult Dengue Infection in 2007

Sompone Punyagupta, M.D., MPH&Trop.Med

## ABSTRACT

In recent years, dengue infection is an emerging disease in adults with all year-round incidence at least in Bangkok and the nearby provinces. The clinical features of 75 patients with laboratory-proven dengue infection who were hospitalized at Vichaiyut Hospital and Medical Center, Thailand from January to June 2007 were described. Clinicians must be well aware that the clinical presentations of adult dengue infection bear some differences from pediatric patients. An initial diagnosis upon hospitalization was correctly made as dengue infection in only 35 patients (46.7%). Severe multiorgan dysfunction was noted in some patients. Caring clinicians must have a high index of suspicion of Dengue infection and should include it in a list of differential diagnosis of acute fever in adult patients. (*J Infect Dis Antimicrob Agents* 2009;26:1-5.)

## INTRODUCTION

Thai hemorrhagic fever has been recognized among Thai children since 1949.<sup>1</sup> A major outbreak started in 1954 and a peak was noted in 1958 with significant mortality of 9.3 percent.<sup>2</sup> Since the causative agent, dengue virus had been isolated and with better understandings on the pathogenesis of dengue hemorrhagic fever (DHF)<sup>3</sup>, the mortality rate reduced to 0.12 percent in another outbreak in 1987. However, since DHF has been signed out as an important disease of children, most of the clinicians and internists are generally not well aware of this disease in adults. In 1975, Srichaikul and colleagues<sup>4</sup>

reported 3 of 9 adult patients with DHF who developed disseminated intravascular coagulation with fatal outcome in two patients. At Vichaiyut Hospital and Medical Center, a 200-bed private hospital in Bangkok, Thailand, we have seen some severe adult patients with DHF from 1983 to 1986 but the cases have rarely been reported since 1986. From 1999 to 2001, there have been only few reports of adult patients with DHF in Thailand.<sup>5-6</sup> In 2002, the Ministry of Public Health<sup>7</sup> reported of 20-30 percent of adult patients with, DHF, in consistent with the observation in Singapore.<sup>8</sup> Recently, we have just reported an adult patient with DHF complicated with multiorgan failure and

---

Vichaiyut Hospital and Medical Center, Setsiri Rd., Phyathai, Bangkok 10400, Thailand.

Received for publication: November 25, 2008.

Reprint request: Sompone Punyagupta, M.D., MPH&Trop.Med, Vichaiyut Hospital and Medical Center, Setsiri Rd., Phyathai, Bangkok 10400, Thailand.

**Keywords:** Dengue infection, Dengue hemorrhagic fever, emerging infectious diseases, adult

hemophagocytic syndrome who was successfully treated with intravenous methylprednisolone and immunoglobulin.<sup>9</sup> We believe that DHF is now a real problem among Thai adults.

### PATIENTS AND METHODS

To confirm the significance of DHF among Thai adults, a retrospective review of adult patients aged of 18 and over who were hospitalized at Vichaiyut Hospital and Medical Center, Bangkok, Thailand, with the clinical diagnosis of DHF and dengue fever (DF) from January 2003 to June 2007 were reviewed. Only 178 (94 males and 84 females) were confirmed by laboratory results positive either dengue IgM antibody, non-structural 1 (NS) antigen, or polymerase chain reaction (PCR).

### RESULTS

#### Demography

During the study period, there were 507 patients with clinical suspicion of dengue infection (248 males and 259 females), but only 178 patients (94 males and 84 females) had proven laboratory results. However, only 75 patients (34 males and 41 females) hospitalized from January to June 2007 had available medical records (Table 1). The disease was more common in

the young age groups (29.3% and 21.3% in the groups of 18-30 and 31-40 years, respectively). However, there was a significant percentage (16.0%) of dengue infection in patients of older than 70 years.

#### Clinical manifestations

The clinical manifestations of all patients with dengue infection are shown in Table 2. The clinical features of dengue infection commonly described in pediatric patients including high fever, generalized myalgia, and severe headache were noted in 74 (98.6%), 48 (64.0%), and 20 (26.6%) patients, respectively, as well as the gastrointestinal symptoms including nausea, vomiting, diarrhea/constipation, and abdominal pain were noted in 22 (29.3%), 12 (16.0%), and 10 (13.3%) patients, respectively. In addition, the respiratory tract symptoms including cough was noted in 10 (13.3%) patients. Petechial rash, shock, and bleeding diathesis were noted in 8 (10.6%), 3 (4.0%), 2 (2.7%) patients, respectively. One patient had a cerebral hemorrhage. An initial diagnosis was correctly made as dengue infection in only 35 (46.7%) patients. Fifty (66.7%) patients were hospitalized within the first three days of illness. Only one patient was afebrile upon hospitalization due to being developing dengue shock syndrome.

**Table 1. Demographic data all 75 adult patients with dengue infection hospitalized from January to June 2007.**

Age (year) \ Sex	18-30	31-40	41-50	51-60	61-70	>70	Total
Male	12	7	3	3	4	5	34
Female	10	9	6	7	2	7	41
Total (%)	22 (29.3)	16 (21.3)	9 (12)	10 (13.3)	6 (8)	12 (16)	75 (100)

### Laboratory results

Table 3 shows the initial laboratory results. Hemoconcentration (hematocrit of more than 40 percent), leucopenia (white blood cell count of less than 4,000 cells/mm<sup>3</sup>), lymphocytosis, and thrombocytopenia (platelet count of less than 100,000 cells/mm<sup>3</sup>) were noted in 49 (65.3%), 62 (82.7%), 66 (88%), and 48 (64%) patients, respectively. Upon hospitalization, mild elevation of transaminases was noted in 42 (56%)

patients, and hypoalbuminemia was noted in 12 (16%) patients. PCR testing for dengue virus serotypes were carried out in only 11 patients, and serotype 4 was the most common causative agent (six patients). There was no serotype 1.

### Treatment and outcome

Intravenous dexamethasone (4 mg every 6 or 8 hours for 2-3 days) was administered without adverse

**Table 2. Major clinical presentations upon hospitalization of 75 adults patients with dengue infection.**

Symptom or sign*	Number (%)
Fever	74 (98.6)
Generalized myalgia	48 (64)
Nausea vomiting	22 (26.6)
Chills	12 (16)
Diarrhea/constipation	12 (16)
Abdominal pain	10 (13.3)
Cough	10 (13.3)
Rash	
- Initial	8 (26.6)
- Subsequent	12 (26.6)
Hypotension	3 (4)
Bleeding diathesis	2 (2.66)
Altered consciousness	1 (1.3)

\*All data were upon hospitalization unless otherwise denoted.

**Table 3. Laboratory results in 75 adult patients with dengue infection.**

Data*	Number (%)
Hematocrit (%)	
> 40	49 (65.3)
35-40	16 (21.3)
< 35	10 (13.3)
Leukocyte count (cells/mm <sup>3</sup> )	
< 4,000	62 (82.7)
4,000-10,000	12 (16)
> 10,000	1 (1.3)
Monocytosis/lymphocytosis	66 (88)
Thrombocytopenia (10,000 cells/mm <sup>3</sup> )	48 (64)
Initial transaminasemia (> 50 units)	42 (56)
Subsequent transaminasemia (> 50 units)	13 (17.3)
Hypoalbuminemia (<6.5 g/dL)	12 (16)

\*All laboratory results were initially performed upon hospitalization unless otherwise denoted.

effects in 32 patients with severe complications, and all of them showed rapid clinical improvement. They were discharged within 3 days of hospitalization, compared to 4-7 days in all except one patients without steroid treatment. There were no mortality in all patients in our study.

## DISCUSSION

There were 75 patients with confirmed laboratory results of dengue infection who were hospitalized in our institute from January to June 2007. During the same period, a total of 5,042 patients were hospitalized. Dengue infection was more prevalent in the young age group (between 18-40 years), however, there were a significant number of patients of more than 70 years. These observations probably indicate the significant role of residential infections. A temperature of more than 38°C was the main symptom upon hospitalization in all patients except one who developed dengue shock syndrome. It is notable that the gastrointestinal symptoms including nausea, vomiting, diarrhea/constipation, and abdominal pain were relatively common, in consistent with those observed in pediatric patients with dengue infection. In addition, approximately one-tenth of patients presented with the respiratory tract symptoms including cough. These presentations may lead caring clinicians to make a wrong diagnosis of common bacterial infections including enteric fever. An initial diagnosis upon hospitalization was correctly made as dengue infection in only 35 (46.7%) patients. Petechial rash commonly noted in pediatric patients was uncommon in our study. Bleeding diathesis and hypotension were also unusual, yet these symptoms indicated the severe form of dengue infection (DHF). Severe headache was noted in 20 (26.6%) patients, and alteration of consciousness was noted in one patient with a cerebral hemorrhage. Neurological complications in dengue infection are

occasionally observed in children.<sup>10-12</sup>

The laboratory findings of hemoconcentration, leukopenia, lymphocytosis, monocytosis, and thrombocytopenia were the major initial laboratory findings in our study.

A mild elevation of transaminases was noted in approximately a half of the patients upon hospitalization, but a significant elevation developed during hospitalization in some patients with gradual resolution within a few months (data not shown). In our study, dengue serotype 4 was the most common causative agent, and there was no serotype 1. However, PCR testing was carried out in only 11 patients. In 2008, dengue serotype 1 was reported in our institute in a dengue patient complicated with multiorgan failure.<sup>13</sup>

Since we consider the fluid leakage and vasculitis as the pathoimmunogenesis in dengue infection, and we have had good experiences in using intravenous corticosteroid and immunoglobulin to many patients with severe dengue infection<sup>4,9,13</sup>, hence we included the results of therapeutic effect of intravenous dexamethasone in our study. Intravenous dexamethasone (4 mg every 6-8 hours for 2-3 days) was administered to 32 patients with severe complications. Eight of these patients required platelet or pack red blood cell transfusion on the first day of hospitalization. A very good and rapid clinical response was observed within 24 hours of the treatment in all patients. Fever was subsided within 1-3 days, and the length of hospital stay was shorter than that in patients without steroid treatment. However, our study was not a randomized controlled design. Therefore, there is a need to perform a randomized controlled study before a recommendation of adjunctive dexamethasone therapy in patients with severe dengue infection. Piankijkam<sup>14</sup> also expressed similar experience with adjunctive corticosteroid treatment in severe dengue infection Siriraj Hospital.<sup>14</sup>

Our study had some limitations. Only 75 patients hospitalized from January to June 2007 were confirmed by laboratory results of dengue infection and had available medical records, even though we try to include all patients hospitalized from 2003 to 2007. Another limitation in our study is the laboratory testing for confirmation of dengue infection. The World Health Organization recommends viral isolation, PCR testing, and serologic studies either hemagglutination inhibition test or enzyme-linked immunosorbant assay for the diagnostic tests of dengue infection. Rapid dengue antibody and antigen tests are unreliable, especially there are no paired sera tested.

In conclusion, there are a significant percentage of dengue infection in adult patients hospitalized with acute febrile illness in our institute. Caring clinicians must have a high index of suspicion of this infection and should include it in a list of differential diagnosis of acute fever in adult patients.

## References

1. Thongcharoen P. Hemorrhagic Fever. Bangkok: Aksornsamai Press, 1977.
2. Nimmannitya S, Halstead SB, Chen SN, Margiotta MR. Dengue and Chikungunya virus infection in man in Thailand 1962-1964. I. Observation on hospitalized patients with hemorrhagic fever. *Am J Trop Med Hyg* 1969;518:954-71.
3. Gubler DJ. Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev* 1998;11:480-96.
4. Srichaikul T, Punyagupta S, Nitiyanant P, Alkarawong K. Disseminated intravascular coagulation in adult Dengue haemorrhagic fever: Report of three cases. *Southeast Asian J Trop Med Public Health* 1975;6: 106-14.
5. Chareonsook O, Foy HM, Teeraratkul A, Silarug N. Changing epidemiology of dengue hemorrhagic fever in Thailand. *Epidemiol Infect* 1999;122:161-6.
6. Rongrungruang Y, Leelarasamee A. Characteristics and outcomes of adult patients with symptomatic dengue virus infections. *J Infect Dis Antimicrob Agents* 2001;18:19-23.
7. จำนวน อึ้งชูศักดิ์. สถานการณ์และแนวโน้มของโรคติดเชื้อไวรัสเด็งกีในประเทศไทย. ใน: ชัยณัฐพันธุ์เจริญ, วันลา กุลวิจิตร, วีระพงษ์ ตันทวีเชียร, อุษา ทิสยากร, บรรณาธิการ. ไข้เลือดออก. กรุงเทพฯ: เพนตากอน แอ็ดเวอรัทซิ่ง, 2546:11-4.
8. Ooi EE, Goh KT, Chee Wang DN. Effect of increasing age on the trend of dengue and dengue hemorrhagic fever in Singapore. *Int J Infect Dis* 2003;7:231-2.
9. Srichaikul T, Punyagupta S, Kanchanapoom T, Chanokovat C, Likittanasombat K, Leelasiri A. Hemophagocytic syndrome in Dengue hemorrhagic fever with severe multiorgan complications. *J Med Assoc Thai* 2008;91:104-9.
10. Kankirawatana P, Chokephaibulkit K, Puthavathana P, Yoksan S, Apintanapong S, Pongthapisit V. Dengue infection presenting with central nervous system manifestation. *J Child Neurol* 2000;15:544-7.
11. Pancharoen C, Thisyakorn U. Neurological manifestations in dengue patients. *Southeast Asian J Trop Med Public Health* 2001;32:341-5.
12. Solomon T, Dung NM, Vaughn DW, et al. Neurological manifestations of dengue infection. *Lancet* 2000;355: 1053-9.
13. Punyagupta S. Multiple Organ Failure Manifestation in Adults with Dengue Infection. The Second International Conference on Dengue and Dengue Hemorrhagic Fever, Oct 16, 2008, Phuket, Thailand.
14. อนงค์ เพียรกิจกรรม. ประสบการณ์ในการวินิจฉัยและรักษาผู้ป่วยไข้เลือดออก: ความรู้ทางโลหิตวิทยาสำหรับแพทย์ทั่วไปและแพทย์เฉพาะทาง กรกฎาคม 2549 หน้า 53-63.