

# DENGUE HEMORRHAGIC FEVER IN INFANCY AT PETCHABUN HOSPITAL, THAILAND

Prasonk Witayathawornwong

Department of Pediatrics, Petchabun Hospital, Petchabun, Thailand

**Abstract.** Prospective study of dengue hemorrhagic fever in infancy at the Pediatric Department, Petchabun Hospital during May 1997 to April 1999 is reported. There were 31 patients (2.9%) from total DHF cases of 1,044. Ten patients from 31 (32.2%) were referred from district hospitals. Male to female ratio was 17 : 14 (1.2 : 1). Maximal, minimal and median ages were 11.5 months, 22 days and 8 months, respectively. All patients had signs, symptoms and laboratory results compatible with dengue hemorrhagic fever. Serologic response was primary dengue infection. Five patients (16.1%) had gastrointestinal hemorrhage, all of them needed blood transfusion. Crystalline solution was fluid of choice given to all patients. Three patients were complicated with febrile convulsions. All patients had rapid and uneventful recovery.

## INTRODUCTION

Dengue hemorrhagic fever (DHF) is an important health problem in Thailand and Southeast Asia (Halstead, 1980) and can be found world wide (Hayes and Gubler, 1992). Most cases were under 15 years of age but under one year was uncommon. The incidence of infant DHF reported was 1.9% (Witayathawornwong, 1993), 1.6% (Pimjaipong *et al*, 1990) and 6.5% (Nimmannitya, 1987). The youngest patient that had been reported was 40 days old (Witayathawornwong, 1993). Dengue infection of a 6-day-old neonate was also reported (Thaithumyanon *et al*, 1994). It was the first report of vertical transmission from a DHF parturient woman. Mean age of infant DHF is about 6 to 8 months (Nimmannitya, 1991), primary dengue infection being the mode of infection.

## MATERIALS AND METHODS

There were 31 infants (2.9%) in a total of 1,044 DHF cases (male : female = 525 : 519) during a 2 year period (May 1997 to April 1999) in Petchabun Hospital, Petchabun, Thailand. They had signs, symptoms and laboratory investigations compatible with DHF (WHO, 1997). All chest radiologic findings

revealed right pleural effusion. Serologic testing by hemagglutination inhibition (HI) showed primary dengue infection.

Vital signs were closely recorded every 1, 2 and 4 hours in the first, second and third 24 hours after onset of fever respectively. Serial hematocrit was done every 4-6 hours or more frequent if necessary in 24-48 hours after fever. Drugs such as steroids, H<sub>2</sub>-blockers, vitamins, antibiotics and vasopressors were not used except acetaminophen for fever and antacid for abdominal pain. Crystalline solutions (5%D/NSS or 5%D/NSS/2) was the fluid of choice in the afebrile phase. Plasma and platelet concentrates were not used. Fresh whole blood (FWB) or packed red cells (PRC) were used for significant hemorrhage. Fluid replacement was adjusted every 6 hours according to vital signs, hematocrit and general condition.

## RESULTS

### Epidemiologic data

There were 31 infants with age range and median of 22 days to 11 months and a half and 8 months respectively. Male to female ratio was 17 : 14 (1.2 : 1). Ten cases (32.2%) were referred from district hospitals without definite diagnosis of DHF. Twenty - six cases (84%)

were found in rainy season from May to October. Fig 1 shows the number of cases by age. The number of cases by district area in Petchabun Province and the reciprocal neutralizing titers of all patients are shown in Figs 2, 3 respectively.

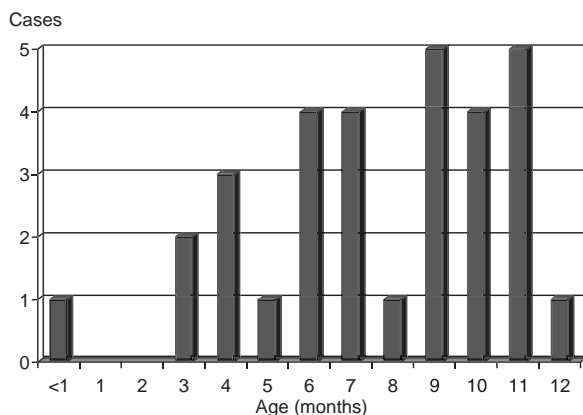


Fig 1—The number of cases by age.

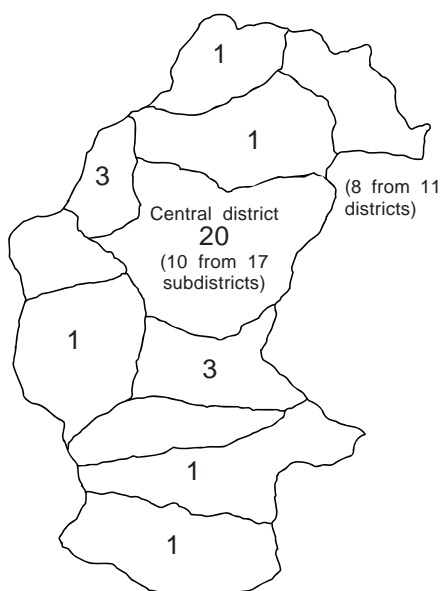


Fig 2—The number of cases by district area in Petchabun Province. Thirty-one infants were found in 8 from 11 districts. Twenty cases were found in Muang or Central district (10 from 17 subdistricts) and 11 cases in 7 other districts. (After this study there were infant DHF cases from three remaining districts).

**Clinical data**

Clinical manifestations and results of laboratory investigations of 31 patients are presented in Figs 4, 5, and Tables 1, 2. Twenty-three from 31 patients (74.2%) had total duration of fever of 4-5 days (Fig 4), 1, 4, 19, 5, 1 and 1 cases had total duration of fever of 3,4,5,6,7 and 8 days respectively.

Right lateral decubitus position of chest X-rays demonstrated pleural effusion of all patients (Fig 5).

Associated diseases and complications were diarrhea (3), vomiting (8), URI (10), thalassemia (2) (spleen not palpated), splenomegaly (1) (not thalassemic case), protein energy malnutrition (5) (Chavalittamrong and Tantivongse, 1987) and G6PD deficiency (1).

**Laboratory investigations (in afebrile phase)**

Table 2 shows results of laboratory investigations of 31 patients.

**Therapy**

All patients (31) received crystalline solutions while 29 patients were treated with 5%D/NSS/2 and 2 patients with 5%D/NSS. The total duration of fluid therapy were 36, 45, 48, 58 and 60 hours in 5, 1, 22, 1 and

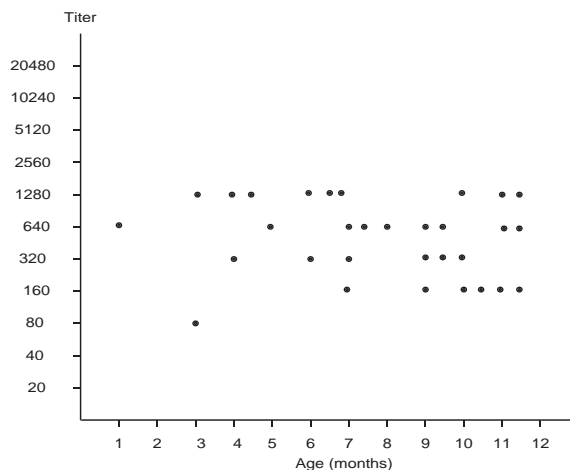


Fig 3—Reciprocal neutralizing (HI) titers of all patients showing primary dengue responses.

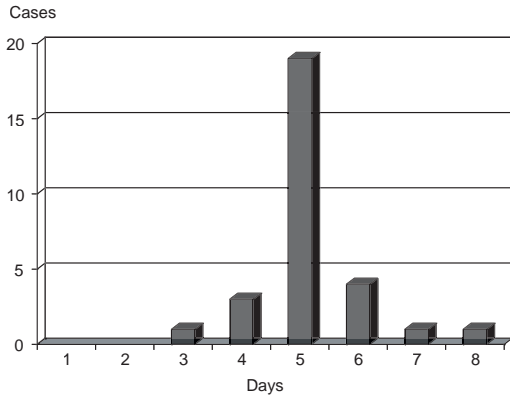


Fig 4—The number of cases by total duration of fever.

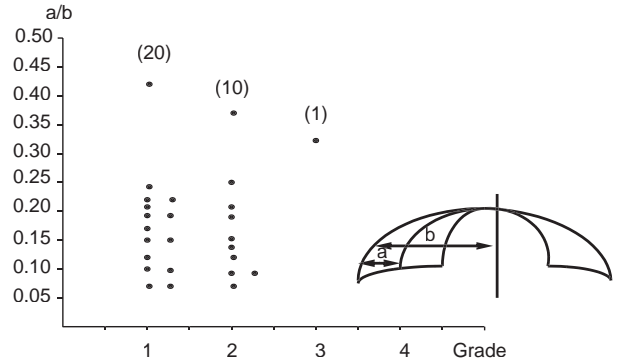


Fig 5—Pleural effusion index.

Table 1  
Clinical manifestations of the patients.

Clinical manifestations	Number of patients (%)
Hematologic manifestations :	
positive tourniquet test	31 (100)
petichiae (generalized)	7 (22.6)
concealed bleeding	3 (9.6)
hematemesis	2 (6.4)
Hepatomegaly :	
just palpable	3 (9.6)
1-2 cm	11 (35.5)
3-4 cm	17 (54.8)
Shock / non shock :	
grade I	20 (64.5)
grade II	10 (32.2)
grade III	1 (3.2)

4 cases respectively. Mean duration was 47.6 hours.

Five patients with internal hemorrhage and one with thalassemia received packed red cell (PRC) transfusion (10 ml/kg).

Maintenance (M) of the total volume of fluid in the first 24 hours after fever was made, maintenance plus 3% deficit (M+3%D) and maintenance plus 5% deficit (M+5%D) were undertaken in 17, 6 and 8 cases respectively.

Details of fluid replacement and results of therapy are presented in Table 3.

Total hospital days were 2, 3, 4 and 5 days respectively. Mean was 3.1 days.

**Detail about 5 patients with internal hemorrhage**

Detail about clinical and epidemiologic

data of 5 patients with internal hemorrhage are shown in Table 4 and laboratory investigations and therapy in afebrile or shock phase are presented in Tables 5 and 6.

**DISCUSSION**

In this study infant patients were 2.9% of total DHF cases, males were slightly more than females. Mean age was 8 months, the common age in this age group (Nimmannitya, 1991). A 22-day-old infant was the youngest patient that had been reported. All patients were found in 8 of 11 districts of Petchabun Province. Twenty patients from Muang or Central district were found in 10 of 17 subdistricts. Older patients (1,013 cases with age range 1-14 years) were found in all subdistricts of all districts of Petchabun Province. This data implied

Table 2  
Complete blood count (CBC), coagulogram, liver enzymes and electrolytes.

Laboratory investigations	Number of patients (%)
Hemoconcentration : increase of hematocrit 11-15%	6 (19.3)
16-20%	5 (16.1)
> 20%	20 (64.5)
Thrombocytopenia (range 14,000 - 99,000/ml, mean 57,000/ml)	31 (100)
White blood cells (WBC) <sup>a</sup> : normal WBC, neutrophils and lymphocytes	27 (83.9)
Coagulogram : normal prothrombin time (PT: 10-14 seconds)	31 (100)
normal partial thromboplastin time (PTT : 25-38 seconds)	26 (83.9)
slightly increased PTT	5 (16.1)
Liver enzymes : abnormal AST (SGOT) : range 36-183 mean 76	31 (100)
abnormal ALT (SGPT) : range 32-65 mean 48	31 (100)
Electrolytes : normal value of sodium <sup>b</sup> and potassium <sup>c</sup>	27 (87.1)
hyponatremia (128,129,130 and 130 mEq/l)	4 (12.9)

<sup>a</sup>Hathirat *et al* (1976); Lukens (1993), <sup>b</sup>135-145 mEq/l, <sup>c</sup>3.5-4.5 mEq/l.

Table 3  
Fluid therapy and results.

Fluid replacement and results	Number of patients (%)
Fluid replacement : Crytalloid - 5% D/NSS/2	29 (93.5)
- 5% D/NSS	2 (6.5)
Blood-PRC 10 ml/kg	6 (19.4)
Total volume of fluid in the first 24 hours after fever : maintenance - M	17 (54.8)
- M + 3% D	6 (19.4)
- M + 5% D	8 (25.8)
Duration of fluid therapy : 36-48 hours	26 (83.9)
48-60 hours	5 (16.1)
Total hospital days : 2-3 days	23 (74.2)
4-5 days	8 (25.8)

Table 4  
Clinical and epidemiologic data.

	Patients				
	1WCh	2SS	3KK	4ThK	5SP
Age/sex/weight (kg)	9m/M/8.0	11m/M/8.5	11m/M/9.0	10m/M/8.0	22d/F/3.5
Admitted day	1/1/97	2 /12/97	18/5/98	4/5/98	27/6/98
Total duration of fever (days)	5	5	5	5	4
Grade/liver (cm)	3/3	2/4	2/just palpable	2/2	2/3
Hematologic manifestations	concealed bleeding	hematemesis	concealed bleeding	concealed bleeding	generalized peti-chiae, hematemesis
Associated diseases/ complications	diarrhea/ febrile convulsion	-	URI/ thalassemia	-	-
Dengue infection	primary	primary	primary	primary	primary
HI titer (1 <sup>st</sup> , 2 <sup>nd</sup> )	1:20, 1:320	1:40, 1:1,280	1:40, 1:640	1:80, 1:1,280	1:80, 1:640

Table 5  
Laboratory investigations and therapy (in afebrile or shock phase).

	Patients				
	1WCh	2SS	3KK	4ThK	5SP
WBC	7,100	21,700	6,700	29,500	18,000
PMN/L/ATL(%)	34/58/5	36/50/3	-/100/-	29/62/2	33/38/21
Platelets	27,000	36,000	99,000	54,000	41,000
Hct (max-min)	36-25	45-27	25-17	35-12	37-28
SGOT/SGPT	120/62	100/58	85/65	102/64	106/56
PT/PTT <sup>a</sup>	14/46	13/45	14/42	13/42	14/46
Na <sup>+</sup> K <sup>+</sup>	128/3.4	136/4.0	129/3.6	130/3.8	130/4.2
Pleural effusion	+	+	+	+	+
Blood transfusion <sup>b</sup>	PRC	PRC	PRC	PRC	PRC
Fluid used	5%D/NSS/2	5%D/NSS/2	5%D/NSS/2	5%D/NSS/2	5%D/NSS/2
Total fluid in 24 hours <sup>c</sup>	M+5%D	M+3%D	M+5%D	M+5%D	M+5%D
Duration of fluid therapy	60 h	45 h	58 h	48 h	60 h
Total hospital days	3	3	3	4	4

<sup>a</sup>PT (10-14 seconds) / PTT (25-38 seconds), <sup>b</sup>10 ml/kg, <sup>c</sup>Total fluid in 24 hours after fever.

Table 6  
Comparison of laboratory investigations between patients with usual manifestations (26) and internal hemorrhage (5).

Laboratory investigations <sup>a</sup>	Usual manifestations (26)	Internal hemorrhage (5)	p-value
SGOT	52.6 (14.4)	102.6 (12.5)	0.007 <sup>b</sup>
SGPT	38.0 (4.2)	61.0 (3.8)	0.001 <sup>b</sup>
PT	11.4 (0.55)	13.6 (0.55)	<0.001 <sup>b</sup>
PTT	36.2 (1.8)	44.2 (2.0)	0.002 <sup>b</sup>
Platelets	67,000 (19,562.7)	55,400 (27,005.5)	0.118
Serum sodium (Na <sup>+</sup> )	136.6 (2.4)	130.6 (3.1)	0.050

<sup>a</sup>mean (standard deviation), <sup>b</sup>significant.

that dengue virus is widespread in this province. Twenty-six patients (84%) were found in the rainy season from May to October, the common epidemic period (Nimmannitya, 1991). Serology of all patients showed primary dengue infection. Although true mechanisms of disease were not elucidated. Epidemiologic data revealed that subneutralizing level of maternal antibody of infants play an important role in the disease mechanism by enhancing growth of dengue virus in mononuclear phagocytic cells (Klicks *et al*, 1988, 1989; Halstead, 1988, 1989; Mady *et al*, 1991; Littua *et al*, 1990). Clinical manifestations and labo-

ratory investigations of all infants were the same as in older children. High continuous fever for 4-5 days was found in 74.2%. Hematologic manifestations gave a positive tourniquet test in all patients and some patients had generalized petichiae and internal bleeding. Hepatomegaly was detected in all patients ranging from just palpable to 4 cm below right costal margin. Splenomegaly was detected in one non-thalassemic patient (3.2%), about 3 cm below left costal margin (liver was 2 cm below right costal margin). Spleens of 6.3% infant patients under 6-months old could be palpated (Nimmannitya *et al*, 1969). There was

only one patient with a short period of shock (grade III).

Hemoconcentration was demonstrated in all patients. Patients with hematocrit increased more than 20% were about 64.5%. Thrombocytopenia was demonstrated in all patients, with a mean value of 57,000/ml<sup>3</sup>. Prolonged fever, thrombocytopenia and pleural effusion without clinical sepsis and pneumonia suggest dengue hemorrhagic fever. All patients in this study had pleural effusion demonstrated on chest X-ray (right lateral decubitus position).

The data showed that diagnosis of young children was not different from older children (WHO, 1997). There were about one-third of infant DHF (10) cases that had been referred from district hospitals without suspicion of DHF. A 22-day-old infant with nasogastric irrigation for gastrointestinal hemorrhage was referred for blood transfusion. Insertion of nasogastric tube in DHF patients should be avoided because it might aggravate gastrointestinal hemorrhage. Although the incidence of DHF in infants was low, severe cases and mortality were rather high in previous studies: 11% (Pimjaipong *et al.*, 1990), 20.8% (Kalayanaroj, 1989) and 50% (Nimmannitya, 1987). These authors explained that very young age might be a risk factor of complication more than in older children. In this study there was no severe case or mortality. There were only one patient with a short period of shock (grade III) and 5 patients with gastrointestinal hemorrhage who needed blood transfusion. All patients received crystalline solution (5%D/NSS or 5%D/NSS/2) for plasma replacement in the first 24 hours after fever.

Mean total duration of fluid replacement and hospital days were 47.6 hours and 3.1 days respectively. No severe outcome of this study might be due to early diagnosis and early proper managements as the principle of DHF managements. The only slightly abnormal value of laboratory investigations (serum sodium, liver enzymes, coagulogram) were consistent with the mild outcome. Coinfections of this study were upper respiratory tract infection, diarrhea and febrile convulsions.

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