Treatment of Dengue Haemorrhagic Fever at Children’s Hospital No. 1, Ho Chi Minh City, Viet Nam, 1991–1996

By
Nguyen Trong Lan*, Nguyen Thanh Hung*, Do Quang Ha**, Bui Thi Mai Phuong*,
Le Bich Lien*, Luong Anh Tuan*, Vu Thi Que Huong**, Lu Thi Minh Hieu*,
Tieu Ngoc Tran*, Le Thi Cam*, and Nguyen Anh Tuan*

*Dengue Haemorrhagic Fever Department, Children’s Hospital No. 1, Ho Chi Minh City, Viet Nam.
**Pasteur Institute, Ho Chi Minh City, Viet Nam.

Abstract
The clinical manifestation, diagnosis, and treatment of dengue haemorrhagic fever (DHF) presented in this communication were based on the data collected at the DHF Department, Children’s Hospital No. 1, Ho Chi Minh City, Viet Nam, during 1991–1996. The principal cause of death in most cases was circulatory failure (hypovolemic shock), thus making an early diagnosis, recognizing the impending shock and treating patients correctly were the best measures to save the life of DHF–afflicted children. At the DHF Department where a great number of DHF patients were seen each year, with these measures the case fatality rate (CFR) of dengue shock syndrome (DSS) was brought down significantly from 12.5% in 1975 to 0.5% in 1993–1995.

Keywords: DF/DHF, hypovolemic shock, case fatality rate, Viet Nam.

Introduction
Dengue haemorrhagic fever (DHF) has been a major public health problem in Viet Nam over the past three decades. DHF outbreaks have occurred every 3–4 years with the highest number being recorded in 1987 – 83 905 cases and 904 deaths(1). The disease has been currently ranked as one of the leading causes of death in children in southern Viet Nam. Although the case fatality rate (CFR) of dengue shock syndrome (DSS) has been reduced significantly during the past ten years, it still remains rather high in some areas of the country. In this paper, some of the experiences in the diagnosis and management of DHF/DSS at the DHF Department, Children’s Hospital No.1, Ho Chi Minh City, have been summarized which can help in further reducing the CFR.

Material and methods

Material and data were summarized from clinical records at the DHF Department, Children’s Hospital No.1, Ho Chi Minh City, from 1991 to 1996. DHF has been clinically diagnosed based on the WHO criteria of 1986(2) and confirmed by virus isolation, serological tests, and, recently, by RT/PCR.

Results and discussion

A total of 19 215 DHF patients were admitted in the Children’s Hospital. The severity of the disease, age-wise distribution, seasonality, and the clinical profile is summed up as follows:

(i) Severity of the disease

The distribution of DHF patients according to the disease severity between 1991 and 1996 is shown in Table 1.

|----------|------|------|------|------|------|------|

The number of patients increased significantly in the rainy season from July to November, with the peak increase in August and September in which there were many severe cases with DSS (Fig. 1).

(ii) Age-wise distribution

Fig. 2 shows the age-wise distribution of DHF patients in 1996. A majority of the DHF cases occurred in children in the age-groups 5–9 years (37.4%) and 10–14 years (28.7%). Among these patients, there were 348 infants (8.6%) which was an interesting group for our study.

(iii) Clinical manifestations of
Treatment of Dengue Haemorrhagic Fever at Children's Hospital No. 1


DHF/DSS

(a) Fever was a major manifestation of DHF and persist for 2-7 days in almost all cases; a few exceptional cases with fever lasted for more than seven days.

(b) The next major manifestation of DHF was haemorrhagic tendency. Spontaneous bleeding in patients older than one-year-old such as petechiae, epitaxis, gum bleeding, gastrointestinal (GI) bleeding (melaena, haematemesis) were seen in 57%, 14%, 7% and 12% of the patients, respectively.

Table 1. Distribution of DHF patients according to the disease severity at DHF Department, 1991 - 1996

<table>
<thead>
<tr>
<th>Year</th>
<th>Grade I (%)</th>
<th>Grade II (%)</th>
<th>Grade III (%)</th>
<th>Grade IV (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>385 (10.3)</td>
<td>2330 (62.7)</td>
<td>969 (26)</td>
<td>29 (0.7)</td>
<td>3713</td>
</tr>
<tr>
<td>1992</td>
<td>333 (8.6)</td>
<td>2580 (60)</td>
<td>1356 (31)</td>
<td>18 (0.4)</td>
<td>4287</td>
</tr>
<tr>
<td>1993</td>
<td>289 (14.3)</td>
<td>1382 (68.7)</td>
<td>513 (25.5)</td>
<td>26 (1.3)</td>
<td>2010</td>
</tr>
<tr>
<td>1994</td>
<td>288 (15.4)</td>
<td>1095 (58.6)</td>
<td>399 (21.3)</td>
<td>85 (4.7)</td>
<td>1867</td>
</tr>
<tr>
<td>1995</td>
<td>362 (10.8)</td>
<td>1973 (59.3)</td>
<td>875 (26.2)</td>
<td>117 (3.5)</td>
<td>3327</td>
</tr>
<tr>
<td>1996</td>
<td>351 (8.7)</td>
<td>2288 (57)</td>
<td>1193 (29.7)</td>
<td>179 (4.4)</td>
<td>4011</td>
</tr>
</tbody>
</table>

Figure 1. Monthly distribution of DHF cases in patients at DHF Department, 1991-1996

Figure 2. Age distribution of DHF patients in 1996
(c) Hepatomegaly was another major clinical manifestation in DHF. It was observed in 86% of the patients of grade I and II and 98% of DSS cases. In 1995, we studied the impact of DHF on the liver function by measuring the transaminase level of 45 DHF patients confirmed by virus isolation and serodiagnosis. Abnormal levels of AST and ALT were seen in 97.7% and 37.7% of these patients, respectively. The fact that the level of AST was higher than that of ALT and the elevation of transaminase was mild to moderate in most cases (<5-fold greater than the normal upper limit for AST and ALT) showed that the involvement of the liver was mild to moderate in most DHF cases. Two patients with dengue encephalopathy (1992) and one patient with encephalopathy, who died of massive gastrointestinal haemorrhage (1995), had unusually high transaminase levels as a sign of acute liver failure(3). Acute liver failure in DHF leading to encephalopathy and death were also reported by other authors(4,5,6). In 1996, we made post-mortem hepatic biopsy of a boy 10-month-old who had died of DSS (grade III) with massive GI bleeding and encephalopathy. His hepatic tissue specimen was later tested at the Pasteur Institute, Paris. The result revealed hepatic necrosis, steatosis, presence of councilman bodies, and PCR in situ–detected serotype DEN–3.

(d) DSS, which is hypovolemic shock, is the main cause leading to death in DHF if it is not recognized early and is not treated correctly. DSS occurred in 23–39% of all the DHF patients. Most cases (85%) went into shock on the 4th or 5th day of the disease when there was a fall in the body temperature.

(e) As mentioned above, infants were an interesting group for this study. In 1996, we had reported the clinical manifestations of 47 infants confirmed by haemaglutination–inhibition test. High fever (100%), subcutaneous petechiae (97%) and hepatomegaly (100%) were the most common signs. GI bleeding was observed in 8.5% of these cases. The rate of
DSS was rather high (53.1%) (Table 2). All these infants suffered from primary dengue infection(7).

**Table 2.** The observed frequency of clinical manifestations of DHF in 47 infants during 1996

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>47</td>
<td>100</td>
</tr>
<tr>
<td>Subcutaneous petechiae</td>
<td>46</td>
<td>97</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>4</td>
<td>8.5</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>47</td>
<td>100</td>
</tr>
<tr>
<td>Shock</td>
<td>25</td>
<td>53.1</td>
</tr>
<tr>
<td>Cough</td>
<td>20</td>
<td>42.4</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>20</td>
<td>42.5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9</td>
<td>19.1</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Neurologic sign (convulsion, coma)</td>
<td>2</td>
<td>4.2</td>
</tr>
</tbody>
</table>

**Diagnosis of DHF/DSS**

The diagnosis of DHF was done on the above-mentioned clinical manifestations and two laboratory findings: haemoconcentration (more than 20% increase in hematocrit) and thrombocytopenia (<100,000/mm). The clinical diagnosis was confirmed by virus isolation, serological tests, and RT/PCR.

**Virus isolation**

In 1995, 105 blood specimens were sent to the Arbovirus Laboratory, Pasteur Institute, Ho Chi Minh City, for virus isolation. Positive results were obtained in 28 cases (27%) which consisted of 19 strains of DEN-1, 7 strains of DEN-2, and 2 strains of DEN-3. According to the results of virus isolation at the Institute during 1987–1996, DEN-2 was the predominant serotype (90.5%) during the largest outbreak in 1987. Thereafter, the serotypes have been changing. DEN-1 was introduced in 1990 and continued to spread during 1991–1996 with a peak in 1993 (62.5%). During this period a low-level transmission of DEN-3 was also documented(8,9).

**Serological test**

In 1991, 216 DHF patients were studied, of whom 87% were found positive by the haemagglutination inhibition (HI) test. The IgM capture ELISA (MAC-ELISA) had a high sensitivity, specificity and positive
predictive value\(^{(10)}\) (76, 82.1 and 96.6% respectively) (Table 3).

**RT/PCR**

This test has been recently introduced as a quick, sensitive and specific method to diagnose DHF\(^{(11)}\). In 1994–1995, we collaborated with the Pasteur Institute in Paris to study the use of RT/PCR to detect the dengue virus genome from the blood of 80 DHF patients to compare with the results of virus isolation by using the c6/36 cells. These results are given in Table 4.

**Table 3.** Sensitivity, specificity and positive predictive value of MAC–ELISA for DHF diagnosis as observed during 1991

<table>
<thead>
<tr>
<th>MAC–ELISA (Acute blood samples)</th>
<th>DHF Grade I, II (n=83)</th>
<th>DHF Grade III, IV (n = 133)</th>
<th>Total (n = 216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>71.6</td>
<td>78.1</td>
<td>76</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>78.2</td>
<td>100</td>
<td>82.1</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>89.5</td>
<td>100</td>
<td>96.6</td>
</tr>
</tbody>
</table>

**Table 4.** Results of virus isolation and RT/PCR, 1994–1995

<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>1994</th>
<th>1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus isolation</td>
<td>5 DEN–2/35 (14%)</td>
<td>4 DEN–2/45 (8%)</td>
</tr>
<tr>
<td>RT/PCR</td>
<td>15 DEN–2/35 (43%)</td>
<td>10 DEN–2/45 (22.2%)</td>
</tr>
</tbody>
</table>

**Case management of DHF/DSS**

The principle of case management of DHF depends on the severity of the disease.

**DHF grade I, II**

When antipyretic was indicated, acetaminophen 10–15 mg/kg every 4–6 hrs was given; the child was sponged with lukewarm water to reduce high fever.

The child was encouraged to eat his favourite foods and drink fruit juices and Oresol solution as much as possible.

The mother was advised how to take care of her child. The mother was advised to take her child to the hospital immediately when any signs and symptoms of impending shock such as excessive vomiting, vomiting with blood, blood in the stool,
abdominal pain, cold extremities, etc., appeared.

For cases which had excessive vomiting, hepatomegaly and abdominal tenderness, high haemoconcentration, gum bleeding or GI bleeding Ringer’s Lactate or Dextrose 5% in normal saline 5–10 ml/kg/hr was given. The rate of infusion was slowed down gradually.

**DSS grade III**

For DSS grade III, 20 ml/kg/hr of Ringer’s Lactate was given. After the child had come out of shock, we slowed down the rate of infusion gradually. If the child was still in shock, we changed to colloid solution (gelatin, dextran 40,70).

**DSS grade IV**

Ringer’s Lactate or colloid solution was given at the loading dose of 20 ml/kg/15 minutes to bring the child out of shock as quickly as possible. The major advantage of gelatin solution is its minimal effect on coagulation and bleeding due to its dilution effect and the relatively low incidence of hypersensitivity reaction as compared with blood. It was for the first time that modified fluid gelatin (MFG) was used to treat 40 patients of DSS in 1992. For 18 of those patients, MFG was used as the only fluid substitute to add to Ringer’s Lactate. In the remaining 22 patients with symptoms of recurrent shock, dextran was added to MFG and no anaphylactic reactions were noticed. Thus, MFG can be used as the first-choice substitute for plasma in the treatment of DSS following the administration of Ringer’s Lactate. If profound or recurrent shock still persisted after the infusion of MFG, the use of dextran was recommended(12).

Vital signs were monitored every 15–30 minutes until the period of shock had disappeared. Hematocrit was examined every 4–6 hrs. In case of prolonged shock, the central venous pressure (CVP) was measured to guide the therapy. Correction of electrolyte and the acid-base balance was also important. Blood infusion was indicated for cases with significant bleeding.

The case fatality rate of DSS at the DHF Department during 1986–1996 is given in Fig. 3. Treatment with the above-mentioned regimen resulted in a significant decline in the CFR of DSS from 12.5% in 1975 to 5.4% in 1986.
and then to 0.5% in 1993. Since then the same trend is being maintained.

In southern Viet Nam, the CFR of DSS cases in some provincial hospitals are still rather high, ranging between 2% and 6.4%. In Malaysia, Lucy C.S. Lum et al. (1997)\(^{(13)}\) reported that the CFR of 48 patients with DSS was 10.4%. In Indonesia, Sumar P. Soedarmo (1997)\(^{(14)}\) has reported an average mortality rate of 3.6% to 5.2% among the hospitalized DHF patients at the Department of Child Health, Dr Cipto Mangunkusumo Hospital, Jakarta. Therefore, we feel that the reduction in the CFR of the DSS cases at our Department was encouraging.

**Conclusion**

DHF has been a major public health problem affecting children in southern Viet Nam. In order to reduce the fatality rate of this disease, making early diagnosis, recognizing the impending shock, and treating the DSS correctly should be recommended to all medical staff everywhere.

**References**


