Dengue and Dengue Haemorrhagic Fever in Children During the 2000 Outbreak in Chittagong, Bangladesh

by
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Abstract
An outbreak of dengue/dengue haemorrhagic fever occurred during 2000 in Chittagong, Bangladesh. A total of 72 children admitted to the Paediatrics ward of the Chittagong Medical College Hospital were evaluated. Sixty-four (89.0%) children came from the Chittagong metropolitan area and the rest 8 (11.0%) from the rural area. The clinical diagnosis of dengue fever (DF) was made in 26 children (36.0%), dengue haemorrhagic fever (DHF) in 36 (50.0%), and dengue shock syndrome (DSS) in 10 children (14.0%) according to WHO case definition. The mean age was 8.4 ± 3.0 years. The distinct features of the present study were: rural occurrence of the disease, which affected malnourished children and more of the students; a higher prevalence of haemorrhagic manifestations and hepatomegaly; jaundice, cough, splenomegaly and encephalopathy; and high PCV in a half and low platelet in one-fourth of the DF patients. The recorded case fatality was 5 (7.0%). It was found that respiratory difficulty, pleural effusion, splenomegaly, tachycardia, low blood pressure, narrow pulse pressure, prolonged capillary refill time, shock, convulsion, coma and platelet count of 100,000/cmm or less were significantly associated with a 5-25 times higher risk of death. Country-specific control measures, case definition, and case management are desirable.

Keywords: DF/DHF, paediatric group, Chittagong, Bangladesh.

Introduction
Globally, more than 2.5 billion people are at risk for dengue/dengue haemorrhagic fever, with 500,000 DHF cases which require hospitalization each year. Of these, 90% are children less than 15 years of age, with the mortality average of 5% of DHF cases(1). There has been a growing proportion of DHF cases and the occurrence of outbreaks has become a regular feature in the WHO South-East Asia Region(2). Dengue was first reported in Bangladesh in 1964 when it was known as “Dacca Fever”(3); since then, it has remained
endemic. The seroprevalence was found to be 13% and DEN-2, DEN-3, and DEN-4 virus serotypes were documented in 1997\textsuperscript{4}. In 2000, a large number of haemorrhagic fever cases were admitted to the Paediatrics and Medicine departments of the Chittagong Medical College Hospital (CMCH), Chittagong, with a similar situation prevailing in Dhaka. It was then declared as an outbreak of dengue at the national level. This outbreak was the first of its kind when 5,551 cases were reported with 93 deaths up to December 2000.

There were 72 children with dengue/dengue haemorrhagic fever admitted to the Paediatrics ward of the CMCH during the outbreak. The current analysis was carried out in order to document the clinical manifestations, and the morbidity and mortality of dengue/dengue haemorrhagic fever in Bangladesh.

**Materials and methods**

All children (n=72) diagnosed as having dengue fever (DF)/dengue haemorrhagic fever (DHF)/dengue shock syndrome (DSS) and aged up to 12 years, admitted in the Paediatrics ward of the CMCH, during August-November 2000 were studied. The clinical details were recorded on admission and followed prospectively till discharge. The diagnosis of DF, DHF and DSS were made according to the WHO guidelines for the treatment of dengue/DHF in small hospitals\textsuperscript{5}.

For all the patients, the total count of white blood cells (TWBC), haemoglobin, PCV by microcentrifuge technique, and absolute platelet counts on a cell counter were done. Serology for dengue antibody was done in all cases using PANBIO INDX Dip-Stick test for dengue fever (ELISA DOT technique) to detect IgM and IgG. Other investigations such as malarial parasite in blood, serum bilirubin, AST, ALT, prothrombin time, creatinine, electrolytes, serum protein, CSF profile, chest-radiograph, ultrasound of chest and abdomen were done whenever it was indicated by the condition of the patient.

The data were computer-processed using SPSS Windows. Univariate and bivariate analyses were done. Relative risk with 95% confidence interval was calculated for predictors of outcome.

**Results**

Among the admitted children, 64 (89%) came from the urban metropolitan area of Chittagong and the rest 8 (11%) from rural areas. The diagnosis of DF was made in 26 (36%) children, DHF in 36 (50%) children and DSS in 10 (14%) children. The age range of patients admitted was 2.5-12 years. The under-5 children constituted 14%, 5-9-years age group 42% and 10-12-years group 44%. The estimated mean age for DF was 9.0+2.8 years; DHF 8.5+3.1 years and DSS 6.6+2.6 years. There were 42 (58%) male and 30 (42%) female children. Forty-eight (67%) children were students, 10 (14%) were pre-school age and the rest were involved in commercial work. Eighty-three per cent of the children were suffering from different grades of malnutrition and 13% belonged to the severe malnutrition status, i.e. less than 60% of the NCHS# standard, but no association between the nutritional status and disease severity was observed.
### Table 1. Clinical manifestations of DF, DHF and DSS patients

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>DF-26(%)</th>
<th>DHF-36(%)</th>
<th>DSS-10 (%)</th>
<th>Total-72(%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration: Fever on admission (days)</td>
<td>4.8 ± 1.8</td>
<td>5.0 ± 2.2</td>
<td>4.1 ± 2.7</td>
<td>4.8 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Total duration: Fever(days)</td>
<td>8.0 ± 2.5</td>
<td>9.5 ± 4.5</td>
<td>6.5 ± 4.9</td>
<td>8.2 ± 3.5</td>
<td>NS</td>
</tr>
<tr>
<td>Headache</td>
<td>22 (85.0)</td>
<td>27 (75.0)</td>
<td>7 (70.0)</td>
<td>56 (78.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Arthralgia/ myalgia</td>
<td>19 (73.0)</td>
<td>28 (78.0)</td>
<td>8 (80.0)</td>
<td>55 (76.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding (any type)</td>
<td>16 (61.5)</td>
<td>36 (100.0)</td>
<td>10 (100.0)</td>
<td>62 (86.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>7 (27.0)</td>
<td>8 (22.0)</td>
<td>2 (20.0)</td>
<td>17 (24.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Skin rash</td>
<td>3 (12.0)</td>
<td>18 (50.0)</td>
<td>6 (60.0)</td>
<td>27 (38.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Sub-conjunctival Haemorrhage</td>
<td>1 (4.0)</td>
<td>3 (8.0)</td>
<td>1 (10.0)</td>
<td>5 (5.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Jaundice</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (10.0)</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>2 (8.0)</td>
<td>1 (3.0)</td>
<td>0 (0)</td>
<td>3 (4.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory difficulty</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (40.0)</td>
<td>4 (6.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>0 (0)</td>
<td>1 (3.0)</td>
<td>1 (10.0)</td>
<td>2 (3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>6 (23.0)</td>
<td>5 (14.0)</td>
<td>3 (30.0)</td>
<td>14 (19.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (15.0)</td>
<td>4 (11.0)</td>
<td>1 (10.0)</td>
<td>9 (13.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal distention</td>
<td>0 (0)</td>
<td>1 (3.0)</td>
<td>1 (10.0)</td>
<td>2 (3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Ascites</td>
<td>0 (0)</td>
<td>1 (3.0)</td>
<td>0 (0)</td>
<td>1 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>0 (0)</td>
<td>26 (72.3)</td>
<td>10 (100.0)</td>
<td>36 (50.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>0 (0)</td>
<td>4 (11.0)</td>
<td>1 (10.0)</td>
<td>5 (7.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>3 (12.0)</td>
<td>10 (28.0)</td>
<td>2 (20.0)</td>
<td>15 (21.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Gum bleeding</td>
<td>4 (16.0)</td>
<td>6 (17.0)</td>
<td>1 (10.0)</td>
<td>10 (16.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Skin bleeding</td>
<td>8 (31.0)</td>
<td>23 (64.0)</td>
<td>8 (80.0)</td>
<td>39 (54.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Malena</td>
<td>2 (8.0)</td>
<td>19 (53.0)</td>
<td>10 (100.0)</td>
<td>31 (43.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hematemesis</td>
<td>5 (19.0)</td>
<td>12 (33.0)</td>
<td>7 (70.0)</td>
<td>24 (33.0)</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>PV Bleeding</td>
<td>0 (0)</td>
<td>2 (6.0)</td>
<td>1 (10.0)</td>
<td>3 (4.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Hematuria</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (10.0)</td>
<td>1 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding Injection site</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (10.0)</td>
<td>1 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Cold clammy skin</td>
<td>2 (8.0)</td>
<td>8 (22.0)</td>
<td>8 (80.0)</td>
<td>18 (25.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>1 (4.0)</td>
<td>7 (19.0)</td>
<td>8 (80.0)</td>
<td>16 (22.0)</td>
<td>&lt;0.00</td>
</tr>
</tbody>
</table>
Dengue and Dengue Haemorrhagic Fever in Children during the 2000 Outbreak in Chittagong, Bangladesh

The clinical features are shown in Table 1. All cases of DF, DHF and DSS had fever of a mean duration of 4.4±1.8 days, 5.0±2.2 days and 4.1±2.7 days respectively. The total days required to become afebrile was 8.0±2.5 days in DF, 9.5±4.5 days in DHF and 6.5±4.9 days in DSS. Headache and arthralgia/myalgia were complained by about 80% of the DF, DHF and DSS cases. Sixty-two (86%) of the patients had different forms of bleeding manifestations.

The other predominant features of DF were skin bleeding in the form of petechie and purpura (32%), retro-orbital pain (27%), diarrhoea (23.0%), vomiting (15%) and skin rash (12%). Thirty-eight per cent of the DF cases had positive tourniquet test.

There was skin rash in about 60% of the DHF and DSS cases. The hepatomegaly and bleeding from skin were found in 72% and 64% of the DHF and 100% and 80% of the DSS cases respectively. There were significant differences between the DSS and DHF patients in the manifestations of respiratory difficulty (40% vs. 0%), malena (100% vs. 53%), haematemesis (70% vs. 33%), cold clammy skin (80% vs. 22%), tachycardia (80% vs. 19%), narrow pulse pressure (80% vs. 0%), prolonged capillary refill time (90% vs. 0%), shock (40% vs. 0%), coma (70% vs. 6%), and tourniquet test (50% vs. 89%). Out of the 8 (11%) convulsive patients, three had febrile convulsion, three had dengue encephalopathy, one had hepatic encephalopathy and one had dyselectrolytemia.

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>DF-26(%)</th>
<th>DHF-36(%)</th>
<th>DSS-10 (%)</th>
<th>Total-72(%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low blood pressure</td>
<td>1 (4.0)</td>
<td>6 (17.0)</td>
<td>4 (40.0)</td>
<td>11 (15.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Narrow pulse pressure</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>8 (80.0)</td>
<td>8 (11.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Prolonged Capillary refill time</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>9 (90.0)</td>
<td>9 (13.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Shock</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (40)</td>
<td>4 (6.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Convulsion</td>
<td>2 (8.0)</td>
<td>3 (8.0)</td>
<td>3 (30.0)</td>
<td>8 (11.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Coma</td>
<td>0 (0)</td>
<td>2 (6.0)</td>
<td>7 (70.0)</td>
<td>9 (13.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Tourniquet test</td>
<td>10 (38.0)</td>
<td>32 (89.0)</td>
<td>5 (50.0)</td>
<td>47 (65.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>PCV(&gt;100000/cmm)</td>
<td>15 (58.0)</td>
<td>27 (75.0)</td>
<td>7 (70.0)</td>
<td>49 (68.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Platelet: &lt;100000/cmm</td>
<td>2 (8.0)</td>
<td>18 (50.0)</td>
<td>7 (70.0)</td>
<td>27 (38.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Total WBC count: Low</td>
<td>5 (19.0)</td>
<td>4 (11.0)</td>
<td>0 (0)</td>
<td>9 (13.0)</td>
<td>NS</td>
</tr>
<tr>
<td>High</td>
<td>0 (0)</td>
<td>29 (84.0)</td>
<td>2 (20.0)</td>
<td>31 (43.0)</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>16 (62.0)</td>
<td>26 (72.0)</td>
<td>7 (70.0)</td>
<td>49 (68.0)</td>
<td></td>
</tr>
<tr>
<td>IgM</td>
<td>15 (58.0)</td>
<td>23 (64.0)</td>
<td>7 (70.0)</td>
<td>45 (63.0)</td>
<td></td>
</tr>
</tbody>
</table>

*P values for DHF/DSS NS: Not significant
A minor proportion of the cases had jaundice (1.5%), cough (4%), pleural effusion (3%), abdominal distention (3%), ascites (1.5%), and splenomegaly (7%). Only 19% of the DF patients had leucopenia, but 15 (58%) and 2 (8%) children suffering from DF had high PCV and thrombocytopenia of 100,000/cmm or less respectively. In contrast about 30% of the children suffering from DHF and DSS had normal PCV; and 50% of DHF and 30% of DSS children had a platelet count of more than 100,000/cmm. The IgM for dengue was positive in 45 (63%) of the children.

There were five deaths giving an overall mortality of 7%. The mortality in DHF was two (5.5%) and that of DSS three (30%) and the difference is very significant (P<0.001). The data were analysed to identify the predictors of outcome and are shown in Table 2 with calculated relative risk and 95% confidence interval. It is evident that respiratory difficulty, pleural effusion, splenomegaly, tachycardia, low blood pressure, narrow pulse pressure, prolonged capillary refill time, shock, convulsion, coma and platelet count of 100,000/cmm or less were significantly associated with a 5-25 times higher risk of death.

## Discussion

This was the first documented epidemic of dengue in Bangladesh and both urban and rural populations were affected. According to the present study, the predominant age group that was affected was 9-12 years which was found to be 5-9 years in the sero-prevalence survey of 1997(4), suggesting that

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Dead (5)</th>
<th>Alive (67)</th>
<th>RR*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory difficulty</td>
<td>2 (40.0)</td>
<td>2 (3.0)</td>
<td>11.33</td>
<td>2.59- 49.69</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>1 (20.0)</td>
<td>1 (1.5)</td>
<td>8.75</td>
<td>1.63 - 47.00</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>2 (40.0)</td>
<td>3 (4.5)</td>
<td>8.93</td>
<td>1.91 - 41.73</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>4 (80.0)</td>
<td>12 (18.0)</td>
<td>14.00</td>
<td>1.68 - 116.61</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Low blood pressure</td>
<td>4 (80.0)</td>
<td>7 (10.5)</td>
<td>22.18</td>
<td>2.73 - 180.27</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Narrow pulse pressure</td>
<td>3 (60.0)</td>
<td>5 (7.5)</td>
<td>12.63</td>
<td>2.35 - 61.33</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Prolonged capillary refill time</td>
<td>3 (60.0)</td>
<td>6 (9.0)</td>
<td>10.50</td>
<td>2.02 -52.52</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Shock</td>
<td>3 (60.0)</td>
<td>1 (1.5)</td>
<td>25.13</td>
<td>5.83 -110.12</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Convulsion</td>
<td>2 (40.0)</td>
<td>6 (9.0)</td>
<td>5.33</td>
<td>1.04 - 27.26</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Coma</td>
<td>3 (60.0)</td>
<td>6 (9.0)</td>
<td>10.50</td>
<td>2.02 - 54.52</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Platelet &lt;100,000/cmm</td>
<td>4 (80.0)</td>
<td>23 (34.0)</td>
<td>6.67</td>
<td>1.04 -56.59</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*RR: Relative risk
the age of infection is progressively increasing in Bangladesh like that in Singapore and Malaysia where dengue has been endemic for several years. In our series most of the children were students, thereby indicating the importance of school environment while mounting control measures. Girls were not affected severely like elsewhere and a sizeable proportion of our children were malnourished. This is contrary to the earlier belief that DSS is rarely seen in clinically-malnourished children.

The distinct features of the present study were the rural occurrence of the disease which affected malnourished and more of the students; a higher prevalence of haemorrhagic manifestations and hepatomegaly; no ecchymoses, jaundice, cough, splenomegaly or encephalopathy; and high PCV in half and low platelet in one-fourth of the DF patients. This highlights the need to study region-specific and even country-specific clinical features in dengue infection.

Splenomegaly was found in 11% of the DHF/DSS children which needs to be interpreted with caution in a malaria-endemic area like Chittagong. In severe falciparum malaria there may be bleeding manifestations and thrombocytopenia. The differentiating features may be high-grade fever along with pallor disproportionate to blood loss. Jaundice was found in one DSS patient who had convulsion, the other cause being excluded, was diagnosed as hepatic encephalopathy. A significantly higher elevation of aspartate aminotransferase (AST) than alanine aminotransferase (ALT) suggests DHF rather than hepatitis A, B, or C virus infection. Hepatitis is usually caused by DEN-3 virus. In an epidemic in Malaysia, eight cases of hepatic encephalopathy were observed. Dengue encephalitis/encephalopathy is an increasingly recognized entity and dengue virus has been isolated in the brain section and in the cerebrospinal fluid. Besides dengue encephalopathy, central nervous system manifestations may be due to intracranial haemorrhage, electrolyte imbalance or hypoxic ischaemic encephalopathy due to profound circulatory failure.

In an endemic area, dengue virus should be considered as a possible aetiological agent in children presenting with encephalitis/encephalopathy.

The overall mortality recorded in the present study was five (7%), which was two (5.5%) for DHF and three (30%) for DSS. It was found to be low in comparison with the mortality of the first epidemic in Bangkok back in 1958. Possibly, the reduced death rate was due to the awareness about the illness and timely and better management. Our case-fatality rate was still higher and one of the reasons could be that our hospital being a tertiary-level health facility, more serious cases were received. It was also found that the presence of factors like respiratory difficulty, pleural effusion, splenomegaly, tachycardia, low blood pressure, narrow pulse pressure, prolonged capillary refill time, shock, convulsion, coma and platelet count of 100,000/cmm or less was found to be significantly associated with a 5-25 times higher risk of death.

DHF/DSS is believed to occur due to the antibody-dependent enhancement of
the secondary infection\cite{18}. It is apprehended that the future epidemics in Bangladesh may be more devastating if control measures and case-management protocols are not developed in a country-specific way, based on the experience of the 2000 epidemic in Chittagong, Bangladesh.

References