DENGUE HEMORRHAGIC FEVER IN THE STATE OF CEARÁ, BRAZIL, 2005.

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ABSTRACT

Dengue is the most common cause of arboviral disease in the world. The aim of this study was to evaluate the clinical manifestations, laboratory features and outcome of dengue hemorrhagic fever. This is a retrospective study including 49 consecutive patients with dengue hemorrhagic fever in Fortaleza, Brazil, between February and August 2005. Statistical analysis was performed through the software SPSS 10.0 for windows. Patients’ mean age was 34.8±16.8 years; 59.2% were female. The main clinical signs and symptoms at admission were: fever (95.9%), headache (91.8%), myalgia (87.8%), abdominal pain (77.5%) and asthenia (73.5%). Hemorrhagic manifestations were present in 29 (59.2%) patients, including petechia (32.7%), gingival bleeding (18.4%), epistaxis (12.2%), ecchymosis (12.2%) and melena (12.2%). The tourniquet test was positive in 3 of 11 patients (27.2%). Platelets count at admission was 82,644±53,147/mm³. All patients presented platelets < 100,000/mm³. There was significant difference between admission and hospital discharge platelets count (82,644±53,147 vs. 146,081±88,999/mm³, p < 0.001). There was significant decrease between admission and hospital discharge haemoglobin and hematocrit (13.5±1.9 vs. 12.7±1.5/mm³, P = 0.002 and 41.0±5.9% vs. 38.6±4.8%, p = 0.001, respectively). All patients received venous hydration with saline solution. The mean infusion used was 2,513±1,065 mL daily. Four patients (8.1%) received blood transfusions and 9 (18.3%) platelets transfusions. Two patients died (4.1%) due to hypovolemic shock. Dengue is an endemic disease in emergent countries, with potential fatal outcome. Signs and symptoms suggestive of dengue hemorrhagic fever must be known by any physician in order to institute early adequate treatment.

INTRODUCTION

Dengue is one of the most important tropical diseases all over the world. There is an estimated 50-100 million dengue infections occurring annually. Dengue is the most common cause of arboviral disease in the world (Farrar et al. 2007). Almost 40% of the world’s population lives now at risk of contracting dengue (Farrar et al. 2007). Symptomatic human infections may range from a mild disease, flu-like syndrome, sometimes associated with rash (dengue fever - DF) to a more severe form of disease associated with plasma leakage, thrombocytopenia, hemorrhage (dengue hemorrhagic fever
- DHF) and/or shock (dengue shock syndrome - DSS). It causes uncomplicated fever and 250,000-500,000 cases of dengue hemorrhagic fever resulting in 25,000 deaths among patients with shock (Gibbons & Vaughn 2002, Gubler & Clark 1997, World Health Organization 1997, Halstead 1997, Monath 1994).

According to the Pan American Health Organization (2007), dengue transmission has increased significantly in the last two decades. It was reported 559,954 cases of dengue and dengue hemorrhagic fever in Brazil in 2007. There are reports of dengue outbreaks in Brazil since the 19th century. In the last two decades there have been many outbreaks in our country, mainly in the large urban centers in Northeast and Southeast regions (Ministério da Saúde 2005). A seroepidemiological random survey performed in Fortaleza, Ceará, Brazil, found positive results in 44% of the studied subjects, and 41% were found in asymptomatic patients (Vasconcelos et al. 1998). The first cases of dengue in the state of Ceará, after the reintroduction of the disease in Brazil, were registered in 1986, with subsequent periodical outbreaks, such as that occurred in 1994 in the city of Fortaleza, with 27033 confirmed cases (Vasconcelos et al. 1995, Secretaria Municipal de Saúde de Fortaleza 2006). In 2005, the period of the study, it were registered 11210 cases of dengue in our city (Secretaria Municipal de Saúde de Fortaleza 2006).

Dengue virus genome is a ~ 11 kb single-strand positive sense RNA with a single open reading frame which encodes a polyprotein precursor of about 3,400 amino acid residues. Proteolytic cleavages generate 10 proteins that are detected in infected cells (C, prM, E, NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5) (Henchal & Putnak 1990). Considering the antigenic variability, dengue viruses are classified into 4 serotypes (DEN-1 to 4). All four serotypes have been associated with dengue hemorrhagic fever, particularly in secondary infections of serotype 2 (Thein et al. 1997, Vaughn et al. 2000). In addition to serotype classification, significant variation in genomic composition among viruses of each serotype allows for a genotype classification (Lindenbach & Rice 2001). Dengue virus is transmitted by mosquitoes *Aedes aegypti* that is the main vector. The mosquito is well adapted to life in urban settings and typically breeds in clean, stagnant water in containers that collect rainwater (Gubler 2002).

The increase of the population provides many susceptible hosts. Uncontrolled urbanization leads to inadequate management of water, providing a range of large water
stores and disposable that allows the larvae growth (Gubler 1989). The only available mean of controlling infections caused by the dengue virus is the elimination of its principal urban vector (Teixeira et al. 2002). Infection with one serotype confers long-term immunity only to that serotype and only a few months immunity to the others (Innis 1995, Guzman & Kouri 2002, Gubler 1998). Secondary infection with another serotype is the main risk factor for the development of dengue hemorrhagic fever and dengue shock syndrome (Innis 1995). Dengue virus antigen has been found in a variety of tissues, predominately the liver and reticuloendothelial system (McBride 2000).

The aim of the study was to evaluate clinical manifestations, laboratory data and mortality of dengue hemorrhagic fever presentation in our region.

MATERIAL AND METHODS

A clinical chart-based, retrospective study with consecutive patients hospitalized with diagnosis of dengue hemorrhagic fever (DHF) at São Jose Infectious Diseases Hospital, Fortaleza, Ceará was conducted from January to June 2005. The protocol of this study was approved by The Ethical Committee of the São José Hospital of Infectious Diseases.

The diagnosis of dengue was based upon the clinical and laboratory findings, including antibodies by using a commercial immunoglobulin IgG and IgM capture enzyme-linked immunosorbent assay (ELISA). Demographic data (age, gender), epidemiological data (duration between onset of symptoms and hospital admission, period of hospital stay) and possible symptoms and findings related to the disease (systolic and diastolic blood pressure, tachycardia, fever, nausea, vomiting, diarrhea, headache, abdominal pain, muscle pain, jaundice, asthenia, anorexia, rash, vertigo, hypotension, petechia, hepatomegaly, epistaxis, gingival bleeding, dyspnea, tachypnea, echimosis, metrorrhagia, hematuria, hematemesis, pleural effusion, ascites, hemoptysis, conjuntival suffusion, splenomegaly and tourniquet test) were recorded. In the laboratory investigation, serum biochemical measurements were assessed including hematocrit, hemoglobin, white blood count, lymphocytes and platelet counts, serum sodium and potassium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, blood urea and albumin levels.

The World Health Organization (1997) grading system was used to classify patient as having DHF. DHF was defined as fever with thrombocytopenia (platelet
count<100,000mm$^3$) and evidence of plasma leakage as manifested by an increase in hematocrit of $\geq 20\%$ during the course of hospitalization$^4$. Microvascular fragility was demonstrated by a positive "tourniquet test"; this test was performed by inflating a blood pressure cuff on the arm to midway between systolic and diastolic blood pressures for five minutes. The skin below the cuff was examined for petechiae, and a finding of greater than 20 petechiae in a one square inch area was considered positive.

The statistical analysis was performed through the softwares SPSS 10.0 (SPSS Inc. Chicago, IL, USA) and Epi Info, 6.04b, 2001 (Centers for Disease Control and Prevention, USA). The quantitative variables were analyzed by student’s test and Mann-Whitney test when appropriate. The results were expressed through tables and summary measures (mean ± standard deviation) in the cases of quantitative variables. The descriptive values below 5% (p value < 0.05) were considered statistically significant.

RESULTS

Forty nine medical records of consecutive patients hospitalized in an Infectious Diseases Hospital with diagnosis of DHF over 6 month period were analyzed. The mean age was 34.8±16.8 years and 29 (59.2%) were female (p = 0.06). The majority of the patients with DHF (85.7%) were from Fortaleza metropolitan area and the others from the countryside. The mean time between the onset of the symptoms and hospital admission was 6.5±2.7 days. The average period of hospital stay was 4.5±2.1 days. Positive dengue serology (IgM) was found in all patients.

The main clinical signs and symptoms presented by the initial evaluation were: fever (95.9%), headache (91.8%), myalgia (87.8%), abdominal pain (77.5%), asthenia (73.5%) anorexia (67.3%), rash (57.1%), nausea (55.1%) and vertigo (44.9%), as can be seen in Table 1.

The hemorrhagic manifestations were present in 59.2% patients as shown in Table 2. The main manifestations were petechia (32.7%), gingival bleeding (18.4%), epistaxis (12.2%), echimosis (12.2%) and melena (12.2%). This was a retrospective study so a tourniquet test was not performed on most of our patients to elicit development of petechia. The tourniquet test was positive in 3 of 11 patients.
Table 1. Clinical characteristics at admission of 49 patients with DHF in Fortaleza, Ceará, Brazil, 2005.

|                                | Mean±SD or n (%) |
|--------------------------------|------------------|
| Age (years)                    | 34.8 ± 16.8      |
| Gender                         |                  |
| Male                           | 20 (40.8)*       |
| Female                         | 29 (59.2)        |
| Onset of symptoms to admission (days) | 6.5±2.7         |
| Length of hospital stay (days)  | 4.5±2.1          |
| SBP (mmHg)                     | 117±20           |
| DBP (mmHg)                     | 73±17            |
| Fever                          | 47 (95.9)        |
| Headache                       | 45 (91.8)        |
| Myalgia                        | 43 (87.8)        |
| Abdominal pain                 | 38 (77.5)        |
| Asthenia                       | 36 (73.5)        |
| Anorexia                       | 33 (67.3)        |
| Rash                           | 28 (57.1)        |
| Nausea                         | 27 (55.1)        |
| Vertigo                        | 22 (44.9)        |
| Vomiting                       | 21 (42.9)        |
| Diarrhea                       | 19 (38.8)        |
| Arthralgia                     | 17 (34.7)        |
| Tachycardia (pulse rate > 100bpm) | 12 (24.4)    |
| Dyspnea                        | 7 (14.3)         |
| Hepatomegaly                   | 7 (14.3)         |
| Pleural effusion               | 4 (8.1)          |
| Ascites                        | 3 (6.1)          |
| Jaundice                       | 2 (4.1)          |
| Splenomegaly                   | 1 (2.0)          |
| Death                          | 2 (4.1)          |

*p = 0.06 (Fischer exact test). Significant p<0.05

The laboratory findings at admission and at hospital discharge are summarized in Table 3. There was significant decrease in hemoglobin and hematocrit levels from 13.5±1.9g/dL and 41.0±5.9% at admission to 12.7±1.5g/dL and 38.6±4.8% at hospital discharge, respectively (p = 0.002 and p = 0.001).
Table 2. Hemorrhagic manifestations observed in 49 patients with DHF in Fortaleza, Ceará, Brazil, 2005.

| Bleeding presentation | Number of patients (%) |
|-----------------------|------------------------|
| Petechia              | 16 (32.7)              |
| Gingival bleeding     | 9 (18.4)               |
| Epistaxis             | 6 (12.2)               |
| Echimosis             | 6 (12.2)               |
| Melena                | 6 (12.2)               |
| Metrorrhagia          | 6 (12.2)               |
| Hematemesis           | 5 (10.2)               |
| Hemoptysis            | 2 (4.1)                |
| Conjuntival suffusion | 2 (4.1)                |

All patients presented platelets count lower than 100,000/mm$^3$ during hospital stay. Those patients were classified as DHF. There was significant difference between admission and hospital discharge platelets count (82,644±53,147 vs. 146,081±88,999/mm$^3$, p < 0.001). Serum creatinine higher than 1.2mg/dL was found in 6.4% of the patients. The aspartate amino transaminase (AST) and alanine amino transaminase (ALT) levels were higher than 45IU/L in 91.7 and 85.4% of the patients, respectively. Serum albumin lower than 3.5mg/dL was found in 66.7% of the patients. Urinary findings as hematuria and urinary protein were observed in 6 patients. Three patients had urinary protein more than 200mg/dL. Laboratorial findings in DHF are shown in Table 4.

One patient (2.0%) presented diffuse gallbladder wall thickening, without calculi, at abdominal ultrasound. Four patients (8.1%) presented pleural effusion, and three (6.1%) with ascites.

All patients received venous hydration with saline fluid. The mean infusion used was 2,513±1,065 mL/daily. Four (8.1%) patients received erythrocyte transfusions and 9 (18.3%) platelets transfusions. Albumin infusion was used in 4 (8.1%) cases and fresh frozen plasma in 1 (2.0%) patient.

Death occurred in 2 cases (4.1%), both due to hypovolemic shock.
**Table 3.** Laboratory findings in patients with DHF in Fortaleza, Ceará, Brazil, 2005.

| Laboratory findings                  | Mean ± SD | p    |
|--------------------------------------|-----------|------|
| **Haemoglobin (g/dL)**               |           |      |
| Admission                            | 13.5±1.9  |      |
| Hospital discharge                   | 12.7±1.5  | 0.002|
| **Hematocrit (%)**                   |           |      |
| Admission                            | 41.0±5.9  |      |
| Hospital discharge                   | 38.6±4.8  | 0.001|
| **White blood count (/mm$^3$)**      |           |      |
| Admission                            | 4,090±1,980|     |
| Hospital discharge                   | 5,149±2,108| 0.002|
| **Lymphocytes (%)**                  |           |      |
| Admission                            | 34.1±18.2 |      |
| Hospital discharge                   | 46.9±11.9 | <0.001|
| **Platelet count (/mm$^3$)**         |           |      |
| Admission                            | 82,644±53,147|      |
| Hospital discharge                   | 146,081±88,999| <0.001|
| **Serum urea (mg/dL)**               |           |      |
| Maximal                              | 22.3±18.2 |      |
| **Serum creatinine (mg/dL)**         |           |      |
| Maximal                              | 0.8±0.7   |      |
| **Serum sodium (mEq/L)**             |           |      |
| Admission                            | 138.9±1.4 |      |
| Minimal                              | 135.8±3.5 | 0.006|
| **Serum potassium (mEq/L)**          |           |      |
| Admission                            | 4.2±0.5   |      |
| Minimal                              | 3.6±0.4   | 0.009|
| **AST (IU/L)**                       |           |      |
| Admission                            | 85±73     |      |
| Maximal                              | 148.9±122.7| 0.05 |
| **ALT (IU/L)**                       |           |      |
| Admission                            | 66±53     |      |
| Maximal                              | 122.4±88.8| 0.007|
| **Serum albumin (g/dL)**             |           |      |
| Admission                            | 3.6±0.5   |      |
| Minimal                              | 3.2±0.8   | 0.003|

SD – standard deviation; AST- aspartate amino transaminase; ALT – alanine amino transaminase. Significant p < 0.05
Table 4. Laboratorial findings of 49 patients with DHF in Fortaleza, Ceará, Brazil, 2005.

| Blood values            | N (%) |
|-------------------------|-------|
| Platelets < 100,000/mm³ | 47 (96) |
| White blood count < 5,000/mm³ | 30 (65.2) |
| Lymphocytes < 1,000/mm³ | 19 (46.3) |
| Creatinine > 1.2mg/dL   | 2 (6.4) |
| Albumin <3.5mg/dl       | 22 (66.7) |
| AST > 45 IU/L           | 33 (91.7) |
| ALT > 45 IU/L           | 35 (85.4) |

**Urinary findings**

|                    |       |
|---------------------|-------|
| Hematuria > 3 cells hpf | 6 (12.2%) |
| Proteinuria > 1+       | 6 (12.2%) |

AST-aspartate aminotransferase; ALT-alanine aminotransferase.

**DISCUSSION**

The present study describes the clinical and laboratory characteristics of dengue hemorrhagic fever in the city of Fortaleza, Ceará, Brazil. As in many other countries in Latin America, Brazilian people have been seriously affected by dengue infections. About 80% of notified dengue cases in the Americas occurred in Brazil, Epidemics of DF reemerged in Brazil in 1981 when an outbreak caused by DEN-1 and DEN-4 viruses occurred in the Northern region. Subsequently, in 1986, the first outbreak of greater proportions caused by DEN-1 occurred in the metropolitan area of Rio de Janeiro and then spreaded towards the urban areas in the Northeast and Midwest regions of Brazil. In 1990, a new epidemic broke up in Rio de Janeiro, now related to the introduction of DEN-2. Since then, with the spread and circulation of more than one serotype, several Brazilian regions have reported outbreaks with severe illness and deaths. Recently, DEN-3 has been isolated in Brazil and has been associated to DHF (Pires Neto et al. 2005, Miagostovich et al. 2002, Figueiredo 2000).

The most susceptible age group to DHF varies from the studies: 21-30 years old in a Bangladesh study (Islan et al. 2006), 31-40 years in a Malaysia study (World Health Organization 2006) and 21-40 years in a Brunei study (Osman et al. 2007). In the present study, the mean age was 34 years old. Osman et al. (2007) found a male:female ratio of 1.5:1, probably because of the high number of men in outdoor occupational activities, with
greater exposure to infected mosquitoes. In the present study we observed a tendency for female gender but the difference was not statistically significant.

Khan et al. (2008) showed that the onset of the symptoms to hospitalization was around 5 days and the time of hospitalization was 4 days. In similar way we observed the mean time between the onset of the symptoms and hospital admission of 6.5 days (range: 2 to 14 days) and the average period of hospital stay was 4.5 days (range: 1 to 10 days).

There are currently no specific clinically useful diagnostic findings, no drugs, no available vaccine (Farrar et al. 2007). The non-specific presentation of infection increases the relevance of laboratory testing for confirming the etiology.

A confirmed diagnosis is established by culture of the virus, polymerase-chain-reaction (PCR) tests, or serologic assays. Cross-reaction with other flaviviruses interferes with serologic testing; particularly the ELISA for IgG, which can be confusing among people previously vaccinated against other flavivirus infections, such as yellow fever and Japanese encephalitis (Schwartz et al. 2000). IgM antibody could be detected in 90 percent of patients (Ying et al. 2007). In the present study, all patients had positive dengue serology (IgM).

The clinical features of dengue vary with the age of the patient. The incubation period ranges from 3 to 14 days, but it is usually 4 to 7 days (Gibbons & Vaughn 2002). Most persons, especially young children, had asymptomatic infections or they present with mild febrile illness in areas where the disease is endemic (Gibbons & Vaughn 2002). Dengue is typically with high fever accompanied by severe headache, incapacitating myalgias and arthralgias, nausea and vomiting, and macular or maculopapular rash. Ying et al. (2007) found the following clinical findings in DF: fever in all patients, headache, myalgia, bone soreness and skin rash more than 50%. Rodrigues et al. (2002) found in DF: retro-orbital pain in 2/3 of the patients, fever, headache, myalgia and arthralgias in one half of the cases, and rash in only 10%. In the present study, the main clinical signs and symptoms presented in DHF were: fever, headache, myalgia, abdominal pain and asthenia in more than 2/3 of the patients. Wichmann et al. (2004) found in DHF the bleeding manifestation in 35% of the patients and Khan et al. (2008) found hemorrhagic manifestations in 13 (13.2%) patients. In the present study, hemorrhagic manifestations
were present in 59% of patients mainly as petechia, gingival bleeding, epistaxis, echimosis and melena.

A positive tourniquet test is incorporated in the WHO clinical case definition of dengue hemorrhagic fever, but the definition differentiates poorly between dengue and dengue hemorrhagic fever and is not specific (Phuong et al. 2004). Wichmann et al. (2004) found positive tourniquet test in 69%. In our study, the tourniquet test was positive in only 3 of 11 patients.

A significant rises of hematocrit levels at admission are found in patients with DHF and this must be due to dehydration and increased vascular permeability that develops rapidly, over a period of hours (Wichmann et al. 2004). In the present study the patients at admission presented hematocrit level of 41% and at discharge was observed a significant decrease in the hematocrit levels to 38.6%. It is possible that hematocrit falls during hospitalization was due to prompt and vigorous intravenous hydration and bleeding manifestations.

Other laboratory findings commonly associated with dengue include neutropenia, relative lymphocytosis, increased concentration of liver enzymes, and thrombocytopenia (Innis 1995). Ying et al. (2007) found leukopenia, thrombocytopenia elevated alanine aminotransferase, and elevated aspartate aminotransferase in more than 2/3 of the cases and hypokalemia in 1/3. Wichmann et al. (2004) found 85,000/mm$^3$ as the median platelet count on admission. In the present study, we found low platelets count at admission in all patients and the mean platelet count level was 82,600/mm$^3$. There was significant difference between admission and hospital discharge platelets counts (82,644 vs. 146,081/mm$^3$, p < 0.001), showing a good clinical outcome. The white blood count and lymphocytes were low at admission in 46.3% of the patients. Liver involvement is a common finding during dengue infection (Wahid et al. 2000). Khan et al. (2008) found serum ALT and AST elevated in 73% and 94.6% of the patients, respectively. In the same way, in the present study, the ALT and AST levels were 85% and 92% of the patients, respectively.

Dengue-induced acute kidney injury (AKI) is a poorly studied complication. Méndez and Gonzáles (2003) found 1.6% of AKI among 617 children with DHF in Colombia. Horvath et al. (1999) reported 74% of proteinuria during a dengue, including a
patient with nephrotic syndrome. Futrakul et al. (1973) reported 71% of albuminuria and 12% of hematuria. All biopsies showed glomerular changes characterized by hypertrophy and hyperplasia of mesangial and endothelial cells, presence of monocyte-like cells in some of the glomerular capillary lumen and focal thickening of the glomerular basement membrane. Immunocomplexes (IgG, IgM or both, and C3) were found at glomerulus and arterioles wall in 10 cases biopsied 2 weeks after the onset of symptoms. Lima et al. (2007) reported a patient who developed AKI due to DHF without hypotension, haemolysis or rhabdomyolysis. The serum creatinine was 9.9 mg/dl, and urinalysis showed hematuria and proteins ++/3. The patients were discharged with normal renal function. This case demonstrates the possibility of direct renal injury due to hemorrhagic dengue. In the present study, serum creatinine equal and higher than 1.2mg/dL was found in only three patients and after hydration one patient normalized the renal function and the other two patients died due to dengue shock syndrome. We also found hematuria and urinary protein in 6 patients.

Khan et al. (2008) showed that hypoabuminemia was present in 14 of the 68 (21.9%) patients. Therefore, in our study the serum albumin lower than 3.5mg/dL was found in two third of the patients. Significantly a lower serum albumin levels in DHF patients is frequent and are consistent with plasma leakage as the major pathophysiology in these patients.

do Vabo et al. (2004) found among 38 patients submitted to abdominal ultrasound diffuse gallbladder wall thickening (47%), abdominal and/or pelvic free fluid in (31%), splenomegaly (29%), hepatomegaly (26%) and perivesicular fluid (26%). Khan et al. (2008) detected ascites on abdominal ultrasound in two patients who fulfilled all the criteria for DHF. In the present study, one patient (2%) presented gallbladder wall thickening, without calculous. Four patients (8.1%) presented pleural effusion and 6.1% ascites. Complications as myocarditis and neurologic abnormalities, such as encephalopathy and neuropathies have been reported (Lum et al. 1993, Sumarmo et al. 1978). These clinical manifestations were not found in this retrospective study.

There are no specific therapeutic agents for DHF. Oral hydration should be early started in patients without shock. Restoration of the volume of circulating plasma represents the base of therapy for dengue shock syndrome. Prompt and correct institution of
fluid replacement is thought to reduce mortality rates due to dengue hemorrhagic fever and dengue shock syndrome (Dung et al. 1999).

Wills et al. (2005) establishes that the cheapest and safest choice, ringer’s lactate, is as effective as either of the colloids for initial resuscitation of children with moderately severe shock. The saline versus albumin fluid evaluation study findings indicates that albumin and normal saline were equally effective for fluid resuscitation (The SAFE Study Investigators 2004). In the present study, the patients received saline fluid infusion in a mean volume of approximately 2,500 mL/daily.

Plasma leakage occurs between three and seven days after the onset of illness and is the most specific and life-threatening feature of DHF. In patients with marked plasma leakage, shock may develop, especially if supportive treatment is delayed. This coincides with severe thrombocytopenia and elevation of amino transferases. Abdominal pain is also reported to precede the onset of plasma leakage in approximately 60 percent of patients with DHF (Guzman & Kouri 2002, Islan et al. 2006, World Health Organization 2006). The presence of persistent vomiting, intense abdominal pain, sudden change from fever to hypothermia, and marked restlessness or lethargy should alert the clinician to possible dengue shock syndrome. This clinical presentation is associated with a case-fatality rate around 10 to 20% even with aggressive therapy (Rigau-Perez et al. 1998). In the present study, two patients (4.1%) died due to dengue shock syndrome.

In conclusion, DHF is an endemic disease in many emerging countries, with potential fatal outcome. Signs and symptoms suggestive of dengue must be known by any physician in order to institute early adequate treatment.

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