Fatal outcomes during dengue fever epidemic in Mato Grosso do Sul, Brazil: a case-series study

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Resumo

No ano de 2007 uma epidemia de dengue assolou o estado de Mato Grosso do Sul, causando aumento de morbimortalidade pela doença. Foi realizado um estudo do tipo série de casos, com informações dos 21 pacientes que morreram em decorrência de dengue, conforme dados das declarações de óbito e registros de manifestações clínicas da doença nos prontuários hospitalares. Dos casos estudados, 11 (52%) eram do sexo feminino e 10 (48%) do masculino. A mediana de idade foi 44 anos. A mediana de dias de internação foi 4 dias. Dos 21 pacientes, 25% permaneceram por 2,5 dias ou menos e 25% por 18 dias ou mais nos serviços de saúde (média geral de 11,4 dias). Compondo as manifestações de gravidade associadas à dengue nos casos estudados, o desconforto respiratório foi o mais registrado, acometendo 20 pacientes (95,2%), seguido de hemorragia, em 15 (71,4%). Doenças pré-existentes, como hipertensão arterial e cardiopatia, constaram em 23,8% dos prontuários analisados.

Palavras-chave: dengue; doenças comunicáveis; mortalidade.

Abstract

In 2007 a dengue epidemic swept through the state of Mato Grosso do Sul, resulting in high rates of morbidity and mortality from the disease. This case-series study was conducted using information from 21 patients who died of dengue, based on data gleaned from death certificates and on clinical manifestations reported in hospital records. Of the cases studied, 11 (52%) were female and 10 (48%) male. Median age was 44 years. Median hospital stay was 4 days. Of the 21 patients, 25% were hospitalized for 2.5 days or fewer and 25% for 18 days or longer (overall mean length of stay, 11.4 days). Among the severe dengue-related manifestations observed, respiratory distress predominated (20 patients, or 95.2%), followed by hemorrhage (15, or 71.4%). Pre-existing conditions, such as hypertension and heart disease, were reported in 23.8% of medical records.

Keywords: dengue; notifiable diseases; mortality.

Introduction

Dengue fever, with its four virus serotypes (DEN1, DEN2, DEN3, and DEN4), is a major arbovirosis among humans, causing epidemics that affect millions around the
In Brazil, its magnitude has varied with the composition of circulating serotypes, clinical and epidemiological features, and particularly the recurrence of epidemics that have struck the entire country, overburdening healthcare services and disrupting the daily lives of patients, with consequent sharp rises in morbidity and mortality rates.

Although dengue fever had swept through the country in the 1990s, data for the subsequent decade remained gloomy. From 1991 to 2000, 1,660,000 cases were reported, with 41 fatal outcomes. From 2001 to May 2010, however, not only did the number of cases increase to four million, but so did the lethality of the disease, with a total of 1,927 deaths.2,3

In the 2007 epidemic, Brazil’s Central-Western region (which includes the state of Mato Grosso do Sul) numbered among high-incidence areas, with 827 cases per 100,000 residents and three detected serotypes (DEN1, DEN2, DEN3). This scenario contrasted with the situation in 2010, when the neighboring states of São Paulo and Minas Gerais, in the Southeastern region, were hardest hit.2,3 In 2010, reported cases outnumbered those from previous years, numbering 830,000 notifications within the first six months. Nonetheless, the simplicity of diagnostic tools (with tourniquet test and blood count as the principal exams) and initial management (hydration) have failed to prevent deaths caused by delayed diagnosis.4

In the absence of clear clinical signs, hematological changes should be viewed as suggestive of the disease and prompt immediate medical attention, since the patient condition can rapidly deteriorate. Although the protocols defined by the Brazilian Ministry of Health are based on clearly detectable signs and symptoms, the evolution of dengue fever does not always fit official descriptions, carrying with it the potential danger of delayed care.5

Although recognizing that early diagnosis based on exams, as advocated by the World Health Organization (WHO), provides good specificity for detection of the disease, Díaz et al.6 point out the disadvantages of the method in terms of sensitivity and proposed a diagnostic model that includes frequently-overlooked symptoms, such as arthralgia and diarrhea, in addition to proposing parameters for blood count evaluation. Another approach intended to reduce diagnostic error is incorporated into the upcoming 2011 WHO classification of diseases, which narrows symptomatic
dengue virus infection down to only two categories—dengue and severe dengue—thus eliminating the current third category of dengue hemorrhagic fever.7

Given the magnitude of the disease, the purpose of this study was to examine the medical records of dengue fever inpatients who died of the disease in the state of Mato Grosso do Sul in 2007, in order to analyze clinical manifestations and characterize the profile of these patients.

Method

This case-series study included all dengue-related deaths that occurred in Mato Grosso do Sul in 2007 for which death certificates cited the disease (whether in classic or hemorrhagic form) as either the primary cause of death or a condition that significantly contributed to the fatal outcome.

Dengue hemorrhagic fever was considered as the cause of death only when literally stated in the death certificates; in the absence of the term “hemorrhagic,” cases were categorized as classic.

Data were collected from eight healthcare services in seven counties. The study was approved by the Research Ethics Committee of the Universidade Federal de Mato Grosso do Sul (UFMS) (permit 1440, of June 2009).

Medical records were the source of data on clinical manifestations that occurred between hospital admission and death. In accordance with the protocols of the Ministry of Health, these records included clinical and laboratory warning signs and shock, which characterize severe cases.8

The data were treated with descriptive statistical analysis and the results were presented as tables. Bioestat 5.0 and Epi Info 3.4.5 software were used for data analysis. Fisher’s test was applied at a significance level of 5% to confirm statistical association.

Results

Of 21 patients, 11 (52%) were female and 10 (48%) were male. Age ranged from 5 to 89 years (median, 44 years). For five patients (23.8%), duration of hospital stay until death was 1 day, whereas the longest stay was 46 days and median hospital stay 4 days. Of the 21 patients, 25% were hospitalized for 2.5 days or less and 25% for 18 days or longer (overall mean length of stay, 11.4 days).
Only 4 patients (19%) were tested for dengue fever while in hospital. Positive results were entered into medical records. Pre-existing diseases were recorded for 13 patients (62%) (Table 1). At any given time during hospitalization, all patients exhibited one or more warning signs, a condition categorized as “yellow-level risk” by the Office of Health Surveillance of the Ministry of Health.

Table 1 – Distribution of fatal cases of dengue fever in 2007, by pre-existing disease or adverse condition on medical records. Mato Grosso do Sul, Brazil, 2010 (n = 21).

<table>
<thead>
<tr>
<th>Pre-existing condition</th>
<th>Patients¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>None</td>
<td>8</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>3</td>
</tr>
<tr>
<td>Cardiopathy</td>
<td>2</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td>2</td>
</tr>
<tr>
<td>Alcohol in bloodstream</td>
<td>2</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1</td>
</tr>
<tr>
<td>Brain tumor</td>
<td>1</td>
</tr>
<tr>
<td>Chronic otitis</td>
<td>1</td>
</tr>
<tr>
<td>Visceral leishmaniasis</td>
<td>1</td>
</tr>
</tbody>
</table>

¹Includes all chronic conditions reported. For some patients, more than one condition was reported.

Among the severe dengue-related manifestations observed, respiratory distress predominated (20 patients, or 95.2%), followed by hemorrhage (15, or 71.4%) (Table 2).

Table 2 – Distribution of fatal cases of dengue fever in 2007, by warning signs on medical records. Mato Grosso do Sul, Brazil, 2010 (n = 21).

<table>
<thead>
<tr>
<th>Warning signs¹</th>
<th>Patients²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>20</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>15</td>
</tr>
<tr>
<td>Reduced diuresis</td>
<td>11</td>
</tr>
<tr>
<td>Restlessness</td>
<td>11</td>
</tr>
<tr>
<td>Abdominal pain or tenderness</td>
<td>7</td>
</tr>
<tr>
<td>Persistent vomiting</td>
<td>6</td>
</tr>
</tbody>
</table>
Hemorrhage types were distributed as follows: skin (6 patients, or 28.5%), oropharynx, hematemesis, and melena (4 patients, or 19.0%, each). Melena was consistently associated with diarrhea and abdominal pain or tenderness. Transvaginal hemorrhage occurred in one woman, in association with ocular hemorrhage and hematemesis.

No association was found between hemorrhage and pre-existing diseases or between hemorrhage and signs of shock (Tables 4 and 5).

According to data from death certificates, 14 patients (67%) had classic dengue and 7 (33%) developed the hemorrhagic form of the disease.

**Discussion**

The distribution of deaths reflects the fact that dengue fever predominates among adults as opposed to younger patients. In fact, only two fatal outcomes were recorded among young individuals (aged 5 and 19 years). A predominance of deaths among adults with the disease has been reported for the Americas, Africa, and Asia, particularly among males aged 20 to 59 years. In contrast, the disease pattern observed in Southeast Asia as late as 2006, revealed predominance among children. The trend towards higher adult mortality began to shift in 2007, although patients older than 20 years continued to predominate in Mato Grosso do Sul in the same year.9,10,11

Median length of hospital stay (4 days) was greater than in a study conducted in Colombia in 2008.12 In the present investigation, the mean length of hospital stay (11.4 days) differed markedly from data found in other studies, possibly because associated pre-existing pathologies predominated in the present sample (in 13 patients or 69.9% of sample). Official Brazilian records reveal shorter hospital stays, averaging only 6.1 days for dengue hemorrhagic fever and 3.4 for classic dengue cases.11 One hypothesis for these differences is that mean age was higher in the present study than those published elsewhere—e.g., 32.8 years in the study conducted by Smith et al.13 in the city of Rio de Janeiro—which increases the likelihood of pre-existing diseases (found in 71.9% of patients in the present study) and therefore the likelihood of longer hospital stays.
Furthermore, the fact that 5 patients died within 24 hours of admission draws attention to the possibility of delayed access to healthcare and late diagnosis among outpatients.

Signs or symptoms of dengue fever were reported in all the records investigated. Pre-existing diseases, such as hypertension and cardiopathies, were reported for a considerable number of patients (23.8%). The use of salicylates, especially as self-medication, and particularly among elderly patients with vascular diseases, has been related to an increased occurrence of severe manifestations of dengue in Brazil.\textsuperscript{14,15} Although the use of salicylates was not investigated in the present study, the medical records reported 23 episodes of hemorrhage, 12 (52%) of which occurred in the digestive system, strikingly similar to the 52.7% rate of hemorrhagic episodes occurring in the same body system reported in a study of dengue fever conducted in Recife, in the Northeastern state of Pernambuco.\textsuperscript{16}

In the present study, hemorrhage was even more frequent, occurring in 15 patients (71.4%)—in 9 (43%) of them on the day before death. This finding is in stark contrast with previous epidemic outbreaks, such as the 1990 dengue epidemic that hit Ribeirão Preto in the neighboring state of São Paulo, for which no episodes of hemorrhage were recorded.\textsuperscript{1}

In the Recife study,\textsuperscript{9} however, hemorrhage was a major clinical event in fatal cases, most often affecting the digestive system. Aspirin has an effective antiplatelet action when administered at daily doses of 30 mg or higher, but gastric discomfort may occur above 300 mg/day.\textsuperscript{17} Typically, daily doses of 100 mg are prescribed,\textsuperscript{18} but the antiplatelet properties can trigger dyscrasia and hemorrhage in patients with dengue. History of acetylsalicylic acid use should therefore be checked in hypertensive patients presenting with dengue fever symptoms, given the potential of the drug to aggravate the clinical condition of patients.

In this study, respiratory distress affected 20 patients (95.2%), manifesting on the day before death in 15 (75%) of these cases, regardless of hemorrhagic episodes. Described as a warning sign in the protocols for dengue diagnosis in Brazil, respiratory distress is associated with pleural effusion resulting from changes in vascular permeability—a basic feature of the pathophysiology of dengue hemorrhagic fever.\textsuperscript{19}

Pleural effusion has been more frequently observed in recent years in cases of dengue fever. More common in the hemorrhagic form of the disease, pleural effusion is
usually subsequent to the defervescence period, even in cases of classic dengue. Its occurrence requires close observation, but straightforward tests, such as ultrasonography and radiography, can ensure early detection and adequate management of patients, precluding poor prognosis.20,21

Díaz et al.6 pointed out that few studies have reported respiratory symptoms among the clinical manifestations of dengue fever, in contrast with their own investigation conducted in Colombia. Although these manifestations may be common to other acute febrile syndromes, their clinical importance should not be overlooked, since they can constitute warning signs of dengue fever.

In the present study, no records were found of fever on the day preceding death. This corroborates Firmida’s view that pleural effusion is a complication secondary to fever and that respiratory distress suggests deterioration of the patient’s clinical condition.20 Nonetheless, no interventions investigating respiratory distress were registered in the records examined in the present study.

References


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