

## Dengue infection in children and adolescents: Clinical profile in a reference hospital in northeast Brazil

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### ABSTRACT

**Introduction:** This study aimed to describe the clinical spectrum of dengue in children and adolescents from a hyperendemic region who were admitted for hospitalization. **Methods:** A retrospective study was conducted on patients diagnosed with dengue infection upon admission to a reference center in Fortaleza, Brazil. **Results:** Of the 84 patients included, 42 underwent confirmatory testing. The main symptoms were fever, abdominal pain and vomiting. The median level of serum aspartate aminotransferase was 143.5±128mg/dL. **Conclusions:** A peculiar clinical profile was evident among children and adolescents with dengue infection in a reference center in northeast Brazil, including gastrointestinal symptoms and liver involvement.

**Keywords:** Dengue fever. Dengue hemorrhagic fever. Clinical profile.

Dengue infection represents a public health problem for urban populations in the tropical and subtropical areas of the world. Brazilians have been affected by serious dengue infections. In recent years, more than 4 million cases have been reported in all 5 Brazilian geographic regions<sup>1</sup>. Although the adult segment is the most affected, dengue infection in children has increased in recent years. This finding suggests that the clinical and epidemiological profiles of dengue have changed and reflects a stronger relationship between its most serious forms and younger age groups<sup>2,3</sup>.

The aim of this study was to describe the clinical spectrum of dengue in children and adolescents living in hyperendemic regions in Brazil who were admitted for hospitalization in a reference center.

This retrospective study took place in Fortaleza (metropolitan area in northeast Brazil) at the Hospital São José de Doenças Infecciosas (HSJDI), the main health care provider for infectious diseases. The study protocol was reviewed and approved by the institution's Ethics Committee (Protocol number 042/2006).

Medical records were reviewed for all patients aged less than 18 years who were admitted to the HSJDI between January 2006

and December 2007 with a diagnosis of dengue infection upon either admission or discharge. An initial diagnosis of dengue infection was defined as a physician's presumptive diagnosis upon admission to the hospital. The final diagnosis was made by the attending physician upon discharge.

Patients with suspected dengue infection were classified further into 2 groups, dengue fever (DF) or dengue hemorrhagic fever and/or dengue shock syndrome (DHF/DSS), according to all available clinical and laboratory data and based on the World Health Organization (WHO) criteria for dengue classification<sup>4</sup>. Based on the definitions proposed by the Brazilian Ministry of Health, a third patient group was classified as dengue infection with complications (DIC)<sup>5</sup>. Confirmed cases of DF, DHF/DSS, or DIC were defined based on the respective clinical profiles along with serological evidence of acute dengue infection (anti-DENV IgM antibody capture assay).

In total, 252 patients were admitted to the HSJDI with suspected dengue infection. We reviewed the medical records of the 84 (33.3%) patients who were aged 18 years or less. Of the 84 patients, 42 (50%) underwent confirmatory testing, and serological evidence of acute dengue infection was observed in 32 (76.1%) patients.

The demographic data are displayed in **Table 1**. Fourteen (16.6%) patients had not received prior institutional care for their illnesses and 57 (67.8%) patients had passed through at least 1 primary or secondary level health unit prior to admission to the HSJDI.

Presumptive diagnosis of dengue infection upon admission was established for 80 (95.2%) of the 84 patients. The remaining 4 patients were presumed to have or were confirmed with a

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TABLE 1 - Demographics of children and adolescents hospitalized with suspected dengue infection.

Parameters	Number = 84	Percentage
Gender		
male	43	51.2
female	41	48.8
Age (years)		
0-2	13	15.5
3-5	13	15.5
6-8	23	27.3
9-11	11	13.1
12-14	13	15.5
15-17	11	13.1
City of residence		
Fortaleza	50	59.5
other	34	40.5

diagnosis of dengue infection upon hospital discharge. DHF/DSS was suspected in 43 (51.2%) patients upon admission. Among the 32 patients with confirmed dengue infection, 14 (43.7%) patients were observed to have DF, and 18 (56.3%) patients were observed to have DHF/DSS, according to the classification of clinical forms of dengue infection that was established upon discharge. No patients were observed to have DIC. The mean time period between the onset of symptoms and hospital admission was  $6.3 \pm 2.2$  days for the patients with confirmed dengue infection. The main signs and symptoms presented by these patients upon admission are summarized in **Table 2**.

Of the 32 patients with confirmed dengue infection, 24 (75%) exhibited platelet counts below  $100,000/\text{mm}^3$ , and 7 (21.8%) had an initial hematocrit measurement above 42% upon admission. Of the 32 patients with confirmed dengue infection, 30 patients were tested at least once for serum albumin; of these, 22 (77.3%) had hypoalbuminemia (albumin  $<3.5\text{g/dL}$ ).

Of the 84 patients with suspected dengue infection upon admission, 80 patients had at least 1 measurement of serum aminotransferases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]). The mean levels of serum AST were  $143.5 \pm 128\text{mg/dL}$  in patients positive for IgM and  $72.1 \pm 66.5\text{mg/dL}$  in patients negative for either IgM or with other pathologies. The mean levels of serum ALT were  $68.1 \pm 65.8\text{mg/dL}$  for patients with positive IgM and  $55.7 \pm 68.3\text{mg/dL}$  for patients negative for IgM or with other pathologies. The serum aminotransferases were analyzed in all 32 patients with confirmed dengue infection. The proportions of patients with serum AST  $>40\text{mg/dL}$  and serum ALT  $>40\text{mg/dL}$  were 96.6% and 70%, respectively.

TABLE 2 - Clinical findings of children and adolescents hospitalized with confirmed dengue infection diagnosis.

Parameters	Number	Percentage
Fever	32	100.0
Abdominal pain	24	75.0
Prostration	23	71.8
Vomiting	23	71.8
Rash	22	68.7
Hemorrhagic manifestation	21	65.6
Headache	20	62.5
Muscle pain	20	62.5
Hepatomegaly	12	37.5
Ocular pain	10	31.2
Pleural effusion	10	31.2
Ascites	9	28.1
Diarrhea	9	28.1
Edema	7	21.8
Joint pain	3	9.3

The tourniquet test was performed on 25 (29.7%) of the 84 patients admitted for suspected dengue infection and was positive in 17 (68%) patients. Among the 32 patients with confirmed dengue infection, the tourniquet test was performed on 11 patients and was positive in 9 (81.8%) patients.

Out of all 84 patients who were admitted with suspected dengue infection, 13 (15.4%) patients received a transfusion of at least 1 blood-based product. Two patients received plasma, 4 received platelets, and 7 received packed red blood cells. Of these 13 patients, 5 patients received more than 1 transfusion. Of the 32 patients with confirmed dengue infection, 7 (21.9%) patients received a transfusion of at least 1 blood-based product, 2 patients received plasma, 3 patients received platelets, and 2 patients received packed red blood cells. Of these 7 patients, 2 patients required more than 1 transfusion.

**Table 3** lists the concordance data between the 2 different classification systems for dengue infection based on either medical diagnosis upon discharge or the WHO definitions. Of the 18 patients with confirmed DHF/DSS infection, 11 (61.1%) patients were classified in agreement with the WHO definitions. An additional 7 DHF/DSS cases would have been classified as DF based on the WHO definitions. Moreover, 6 of the 14 patients with confirmed DF infection were classified in agreement with the WHO definitions. Finally, 8 DF patients would have been classified as DHF/DSS or DIC according to the WHO definitions.

Of the 84 patients evaluated, 2 patients required treatment in the intensive care unit, 78 patients were discharged, and 6 patients were transferred to other hospitals. Of the 32 cases

TABLE 3 - Classification of children and adolescents hospitalized with confirmed dengue infection according to both medical diagnosis upon discharge and WHO definitions.

Parameters	DF		DHF		DIC		Total	
	n	%	n	%	n	%	n	%
Concordance with WHO	6	42.8	11	61.1	0	0.0	17	53.1
Non-concordance with WHO	8	57.2	7	38.9	0	0.0	15	46.9
Total (medical diagnosis)	14	43.7	18	56.3	0	0.0	32	100.0

DF: dengue fever; DHF: dengue hemorrhagic fever; DIC: dengue infection with complications; WHO: World Health Organization.

confirmed serologically, 31 patients were discharged, and 1 patient was transferred. No deaths occurred.

This study presents a detailed description of the clinical manifestations of dengue infection in children and adolescents who were admitted to an infectious disease reference hospital in northeast Brazil. As information regarding the clinical manifestations of dengue infection in the Brazilian pediatric population is scarce in the literature, these findings are important<sup>2,3,6</sup>. Moreover, most dengue infections that occur in children and adolescents in a community setting manifest as asymptomatic or oligosymptomatic<sup>7</sup>.

In this study, the main, initial clinical signs and symptoms presented by children and adolescents hospitalized with confirmed dengue infection were fairly nonspecific, as was demonstrated in other studies<sup>7,8</sup>.

The gastrointestinal symptoms were remarkable in the children and adolescents analyzed in this study. These findings are similar to a retrospective study originating from Delhi, India, where 134 hospitalized children with clinically suspected dengue infection demonstrated abdominal pain (49%) and vomiting (68%) as common symptoms<sup>9</sup>.

Bleeding manifestations were observed in the majority of children and adolescents with confirmed dengue infection in this study. Hayes et al.<sup>10</sup> evaluated 517 patients with confirmed dengue infection from a hospital in Manila, Philippines, and observed that most (78%) patients were aged less than 15 years (only 3 infants), and some type of hemorrhagic finding had occurred in 460 (89%) cases. Among these patients with bleeding manifestations, only 110 patients were observed to have DHF, whereas the rest were observed to have DF with hemorrhagic manifestations. Gastrointestinal bleeding was present in 65 cases, but only 2 patients developed shock, and no fatalities occurred. Kabra et al.<sup>11</sup> evaluated children and adolescents who were admitted in a hospital in India with a clinical diagnosis of dengue infection. They observed that in dengue shock syndrome patients, hematemeses was present in 55 (49%) patients, epistaxis in 39 (35%) patients, melena in 27 (24%) patients, and ecchymosis in 34 (30%) patients. Another study originating in Jaipur, India, included a total of 948 children who were hospitalized at a tertiary care center with a dengue diagnosis. Bleeding manifestations were observed in 44.5% of these cases. A positive tourniquet test was the most common manifestation and was observed in 300 (31.6%) cases, whereas

bleeding was the only manifestation in 9.2% of the cases. The most common spontaneous bleeding manifestation was epistaxis (25%)<sup>12</sup>. As observed in our study and reported in the literature, bleeding manifestations in children and adolescents with dengue infection may vary according to geographic regions.

Laboratory parameters that are used regularly to evaluate plasma leakage in dengue infection yielded distinct results in this study. Only 21.8% of children and adolescents with confirmed dengue infection had initial hematocrit measurements above 42% at admission, whereas 77.3% presented with hypoalbuminemia.

Remarkable liver involvement was observed in this study. These data are similar to the results described by Mohan et al.<sup>13</sup>, with the exception of jaundice. Mohan et al. evaluated the hepatic function of 61 children who were diagnosed with dengue infection. Hepatomegaly was observed in 74% of the cases and jaundice in 25% of cases. Upon admission, the levels of AST, ALT, and serum alkaline phosphatase were elevated in 87% of children with hepatomegaly and in 81% of children without hepatomegaly. Hepatic dysfunction is a well-recognized feature of dengue infection and often manifests as hepatomegaly and mild to moderate increases in transaminase levels; jaundice and acute liver failure generally occur less commonly<sup>14</sup>. Kabra et al.<sup>11</sup> evaluated 240 children aged between 4 months and 13 years who were admitted to a hospital in India with a clinical diagnosis of dengue infection. The authors observed that unusual clinical features such as jaundice were present in 7 (6%) cases, and hepatic encephalopathy was observed in 6 (5%) cases. Liver pathogenesis can result from dengue infection because of one or more of several potential insults, including direct viral or host immune response effects, on liver cells, compromised circulation and/or hypoxia caused by hypotension, localized vascular leakage inside the liver capsule, hepatotoxic effects of drugs such as acetaminophen, and the specific tissue tropisms of some viral serotypes or genotypes<sup>15</sup>.

Information on the use of blood transfusion products in children with dengue infection is scarce in the literature. In this study, the transfusion of at least 1 blood-based product was relatively common (15.4%) in patients admitted for suspected dengue infection, and 5 patients received more than 1 transfusion.

In this study, poor concordance existed between the classifications of dengue infection based on the medical

diagnosis upon discharge and the WHO definitions. The reasons for low concordance between the medical diagnosis and the WHO classification are unknown; however, it appears that physicians have not applied a consistent and/or precise method to frame the signs and symptoms of dengue infection, which suggests a lack in knowledge regarding the criteria for dengue classification.

Despite limitations such as small sample size and the use of a single hospital for a retrospective analysis, this study concludes that a peculiar clinical profile is presented by children and adolescents with dengue infection at a reference center in northeast Brazil. In this setting, remarkable gastrointestinal symptoms and liver involvement were observed. To facilitate early and appropriate treatment and improved outcomes, physicians should be made aware of the clinical characteristics of dengue infection in children and adolescents.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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