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ORIGINAL ARTICLE

Clinical and laboratory signs associated to serious dengue disease in hospitalized children☆

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KEYWORDS
Dengue;
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Abstract
Objective: To evaluate the validity of clinical and laboratory signs to serious dengue disease in hospitalized children.
Methods: Retrospective cohort of children (<18 years) hospitalized with dengue diagnosis (2007–2008). Serious dengue disease was defined as death or use of advanced life support therapy. Accuracy measures and area under the receiver operating characteristic curve were calculated.
Results: Of the total ($n = 145$), 53.1% were female, 69% aged 2–11 years, and 15.9% evolved to the worse outcome. Lethargy had the best accuracy (positive likelihood ratio >19 and negative likelihood ratio <0.6). Pleural effusion and abdominal distension had higher sensitivity (82.6%). History of bleeding (epistaxis, gingival or gastrointestinal bleeding) and severe hemorrhage (pulmonary or gastrointestinal bleeding) in physical examination were more frequent in serious dengue disease ($p < 0.01$), but with poor accuracy (positive likelihood ratio = 1.89 and 3.89; negative likelihood ratio = 0.53 and 0.60, respectively). Serum albumin was lower in serious dengue forms ($p < 0.01$). Despite statistical significance ($p < 0.05$), both groups presented thrombocytopenia. Platelets count, hematocrit, and hemoglobin parameters had area under the curve <0.5.
Conclusions: Lethargy, abdominal distension, pleural effusion, and hypoalbuminemia were the best clinical and laboratorial markers of serious dengue disease in hospitalized children, while bleeding, severe hemorrhage, hemoconcentration and thrombocytopenia did not reach adequate diagnostic accuracy. In pediatric referral hospitals, the absence of hemoconcentration

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does not imply absence of plasma leakage, particularly in children with previous fluid replacement. These findings may contribute to the clinical management of dengue in children at referral hospitals.

PALAVRAS-CHAVE
Dengue;
Crianças;
Sensibilidade e especificidade;
Estudos de validação

Sinais clínicos e laboratoriais para o dengue com evolução grave em crianças hospitalizadas

Resumo

Objetivo: Avaliar a validade dos sinais clínicos e laboratoriais para o dengue com evolução grave em crianças hospitalizadas.

Métodos: Coorte retrospectivo de crianças (<18 anos) internadas com dengue (2007–2008). Evolução grave foi definida como óbito ou pelo uso de terapia de suporte avançado de vida. Foram calculadas medidas de acurácia e área sob a curva ROC.

Resultados: Do total (n = 145), 53,1% casos eram do sexo feminino, 69% de 2 a 11 anos e 15,9% evoluíram para gravidade. Letargia obteve a melhor acurácia (razão de verossimilhança positiva RVP > 19 e RV negativa RVN < 0,6). Derrame pleural e distensão abdominal apresentaram maior sensibilidade (se = 82,6%). Relato de sangramentos (epistaxe, gengivorragia ou gastrointestinal) e hemorragia grave (pulmonar ou gastrointestinal) presente no exame físico foram mais frequentes nos casos com evolução grave (p <0,01), porém com baixa acurácia (RVP = 1,89 e 3,89; RVN = 0,53 e 0,60, respectivamente). Os níveis de albumina sérica foram mais baixos nas formas graves (p <0,01). Ambos os grupos apresentaram trombocitopenia, apesar da diferença estatística (p <0,05). Contagem de plaquetas, hematócrito e hemoglobina apresentaram área sob a curva ROC < 0,5.

Conclusões: Letargia, distensão abdominal, derrame pleural e hipoalbuminemia foram os melhores marcadores clínicos e laboratoriais de dengue com evolução grave em crianças hospitalizadas, enquanto sangramento, hemorragia grave, hemoconcentração e trombocitopenia não tiveram boa acurácia diagnóstica. Em hospitais de referência pediátricos, a ausência de hemoconcentração não implica ausência de extravasamento plasmático, particularmente quando há reposição anterior de volume. Esses resultados podem contribuir para o manejo clínico do dengue em crianças em hospitais de referência.

Introduction

Dengue is an acute febrile disease caused by a flavivirus, with four known serotypes (DENV-1, DENV-2, DENV-3, and DENV-4). In 2013, the worldwide estimate of dengue infection was 390 million people, 96 million of whom were symptomatic.[1] In Brazil, from 2000 to 2010, there was an increase in dengue incidence, accompanied by a proportional increase in severe cases.[2] Dengue has mainly affected the adult population in Brazil, but the epidemic in 2008 showed an increased incidence in individuals under 15 years of age, with a higher proportion of severe cases in this age group.[2]

The four serotypes can lead to variable clinical presentations, ranging from asymptomatic to severe forms. Infants and preschoolers frequently present an undifferentiated febrile disease. Coryza, seizures, nausea, vomiting, exanthema, and petechiae are more frequent in children under 2 years of age.[3] Children with dengue could evolve into severe forms faster than adults, especially those under 5 years.[4] Signs of hypoperfusion like cold skin, oliguria, and slow capillary refill can appear suddenly after a few days of the febrile phase.[5]

In 1997, the World Health Organization (WHO) established a classification of dengue cases: dengue fever (DF) and dengue hemorrhagic fever (DHF). DHF is subdivided into four stages of severity; stages III and IV are defined as dengue shock syndrome (DSS). In 2009, the WHO proposed a new classification, dengue and serious dengue, in which dengue is subdivided according to the presence or absence of the following warning signs: abdominal pain, persistent vomiting, edema, mucosal bleeding, lethargy, irritability, hepatomegaly (>2 cm), and increased hematocrit concurrent with decreased platelet count.[6] This new classification aimed at simplification and changed the focus from hemorrhage to plasma leakage, the principal factor in pathogenesis of the severe forms.[7]

The WHO and Brazilian Ministry of Health adopted the use of warning signs for clinical case management,[6,8] although their evidence as predictors of severity is not consistent, especially in children.[9] Signs and symptoms most frequently associated with severity in children were: spontaneous