Journal of Microbiology, Immunology and Infection (2013) 46, 271–281

Available online at www.sciencedirect.com

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journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Comparisons of dengue illness classified based on the 1997 and 2009 World Health Organization dengue classification schemes

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Received 24 February 2012; received in revised form 1 June 2012; accepted 10 July 2012

KEYWORDS
Classification schemes;
Dengue fever;
Dengue hemorrhagic fever;
Warning signs;
World Health Organization

Background/Purpose: Dengue cases, traditionally classified as dengue fever (DF) or dengue hemorrhagic fever (DHF) by the World Health Organization (WHO) dengue classification 1997 scheme, are categorized into Group A (without warning signs), Group B [with warning signs (e.g., abdominal pain/vomiting/fluid accumulation/mucosal bleeding/lethargy/liver enlargement/increasing hematocrit with decreasing platelets)], or Group C (severe plasma leakage/severe bleeding/organ failure) by the WHO 2009 version. We compared differences in clinical/laboratory features between patients separately classified as DF/DHF and in Group A/B/C.

Methods: We performed a retrospective analysis of dengue patients diagnosed between 2008 and 2010.

Results: A total of 148 adult patients (119 DF/29 DHF; 64 Group A/77 Group B/7 Group C) were included. Compared with DF, significantly younger age, lower hospitalization rate, and higher platelet count were found in Group A. Compared with DHF, higher platelet count was found in Group B. Six of seven patients (86%) classified as Group C fulfilled the criteria of DHF. A cross tabulation showed DF cases were distributed in all of the severity groups stratified by the WHO dengue 2009 scheme (53.8% Group A/45.4% Group B/0.8% Group C); of the DHF cases, 23 (79%) were categorized as Group B, and six (20.7%) as Group C. All patients in Group A fell into the category DF.

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http://dx.doi.org/10.1016/j.jmii.2012.07.005

Conclusion: The WHO 2009 scheme is effective in identifying severe dengue cases. Heterogeneity in severity suggests careful severity discrimination in patients classified in Group B is needed. Our data suggest that it is safe to treat patients classified as Group A on an outpatient basis.

Introduction

Dengue is the most prevalent mosquito-borne viral infection and a major public health problem in the world, with approximately 2.5 billion people living in dengue endemic areas worldwide, and 50 million dengue infections occurring annually.[1–3] The conventional classification of dengue illness as dengue fever (DF) or dengue hemorrhagic fever (DHF) put forward by the World health organization (WHO) in 1975 was based on the results of studies in pediatric patients conducted at the Children's Hospital, Bangkok, Thailand.[4] The diagnosis of DHF established in dengue infection required the fulfillment of all of the following criteria: fever, hemorrhagia, thrombocytopenia ($<100 \times 10^9$ cells/L) and clinical evidence of plasma leakage resulting from increased vascular permeability.[5] The severity of DHF was categorized as follows: Grade I = fever accompanied by non-specific constitutional symptoms with the only hemorrhagic manifestation being a positive tourniquet test result; Grade II = spontaneous bleeding is observed, in addition to the manifestations of Grade I; Grade III = circulatory failure manifested by rapid and weak pulse and narrowing of pulse pressure or hypotension, with the presence of cold clammy skin; and Grade IV = profound shock with undetectable blood pressure and pulse. Grades III and IV were categorized as dengue shock syndrome (DSS).[5] Over the past decades, dengue has geographically expanded and increasingly affected adult populations.[1–3,6–10] A wide variety of dengue clinical manifestations have continuously been unveiled, adding to the major dengue presentations that were initially conceived to be mainly confined to fever and hemorrhagia.[11–13] Of note, It has been increasingly reported that severe dengue might not fulfill the criteria of DHF/DSS, yet put affected patients at high risk for mortality.[14–19] Numerous reports on critically ill dengue affected patients who died of causes other than DHF/DSS have urged for a revision of the convention WHO dengue classification, so that it could elicit practical warning signs in a timely fashion and provide appropriate treatment guidelines for severe dengue.[11–13,20–24] For practical reasons, the latest WHO dengue classification scheme issued in 2009 stratified dengue-affected patients, based on the clinical manifestations, laboratory parameters and the clinical-service delivery, into severe dengue and non-severe dengue cases.[1] However, the usefulness of WHO dengue classification 2009 scheme has not yet been fully evaluated.[1] Taiwanese clinicians are particularly inexperienced with the WHO 2009 dengue classification and treatment guidelines as most of the large dengue epidemics in Taiwan occurred before 2009.[24,25] The aim of this study was to evaluate the difference in clinical and laboratory features between patients who were separately classified based on the WHO classification 1997 and 2009 schemes, and the implications of these differences will be discussed.

Materials and methods

Patients and definitions

Patients with a diagnosis of acute dengue virus (DENV) infection admitted to Kaohsiung Chang Gung Memorial Hospital (KSCGMH), a 2700-bed medical facility serving as a primary and tertiary referral center in southern Taiwan, between 2008 and 2010 were included for retrospective analysis. The medical charts of the included patients were reviewed for retrieval of demographic, clinical, laboratory and imaging information. All included dengue cases were confirmed by at least one of the following criteria: (i) a positive reverse transcriptase-polymerase chain reaction (RT-PCR) result in acute-phase serum, (ii) a positive result for specific immunoglobulin M antibody in acute-phase serum, (iii) a fourfold increase in dengue-specific hemagglutination inhibition titer in convalescent serum as compared with that in acute–phase, and (iv) a dengue-specific nonstructural glycoprotein NS1 detected in acute-phase serum.[26–28] These diagnostic tests were performed by the Taiwan Center for Disease Control (CDC, Taiwan).

All included patients had their blood sampled for the assay of hemogram upon their arrival at KSCGMH. Additional blood chemistry and follow-up hemogram tests during hospital stay were carried out at the discretion of his or her physician as was clinically indicated. An organ impairment in the dengue-affected patient referred to any of the following clinical conditions: pulmonary edema, respiratory failure, severe gastrointestinal tract bleeding, severe hepatitis and rhabdomyolysis.[1] Severe hepatitis was defined as an elevated alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) >1000 U/L [normal range (NR), ALT and AST, <40 U/L],[1] rhabdomyolysis are five or more times the upper limit of normal serum creatine kinase (NR, 20–130 U/L) and/or presence of myoglobin in the blood and/or urine,[29] and severe gastrointestinal bleeding as the passage of large amount of tarry or bloody stool coupled with hemodynamic instability and/or rapid decrease in hemoglobin level.[13] Plasma leakage referred to the presence of pleural effusion, ascites, and/or