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Differences in clinical and laboratory characteristics and disease severity between children and adults with dengue virus infection in Taiwan, 2002

Chin-Chou Wang[a,b], Ing-Kit Lee[c], Mao-Chang Su[a], Hung-I Lin[d], Yi-Chuan Huang[e], Shih-Feng Liu[a], Chao-Chien Wu[a], Meng-Chih Lin[a,*]

[a] *Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Chang Gung Memorial Hospital, Kaohsiung Medical Center, Chang Gung University College of Medicine, 123 Dabi Road, Niaosung Shiang, Kaohsiung, Taiwan*
[b] *Graduate Institute of Occupational Safety and Health, Kaohsiung Medical University, Kaohsiung, Taiwan*
[c] *Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital, Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan*
[d] *Department of Pediatrics, Kaohsiung Municipal Min-Sheng Hospital, Kaohsiung, Taiwan*
[e] *Division of Infectious Diseases, Department of Pediatrics, Chang Gung Memorial Hospital, Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan*

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Summary To compare the clinical and laboratory characteristics and disease severity between adults and children with dengue in Taiwan in 2002, we retrospectively studied 661 serologically confirmed dengue-infected patients (606 adults and 55 children) admitted between June and December 2002 to a single medical centre. The medical charts of the patients were reviewed for demographic, clinical, laboratory and imaging information. Compared with children, adult patients were found to have: higher incidences of arthralgia ($P < 0.001$), myalgia ($P = 0.002$), headache ($P = 0.028$), abdominal pain ($P = 0.004$) and upper gastrointestinal bleeding ($P = 0.013$); lower platelet counts ($P < 0.001$), prothrombin time ($P = 0.030$) and serum albumin levels ($P = 0.037$); a higher incidence of elevated alanine aminotransferase levels ($P = 0.001$); and a higher prevalence of dengue haemorrhagic fever (DHF) (14.4% vs. 3.6%; $P = 0.026$). The current data showed differences in clinical manifestations and laboratory characteristics between children and adults with dengue virus infection. Notably, a higher incidence of DHF was observed in adult patients compared with children in the 2002 dengue epidemic in Taiwan.

* Corresponding author. Tel.: +886 7 731 7123x8199; fax: +886 7 732 2402.
E-mail address: mengchih@adm.cgmh.org.tw (M.-C. Lin).

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1. Introduction

Dengue is the most important mosquito-borne viral disease worldwide and is a major public health concern in tropical and subtropical regions.[1,2] Dengue is an acute febrile illness caused by any one of four dengue virus serotypes (DENV-1, DENV-2, DENV-3 or DENV-4). The clinical manifestations of dengue illness are classified as either dengue fever (DF) or its more severe clinical form, dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS).[3]

In Taiwan, a number of dengue epidemics have occurred over several decades.[4] A dengue epidemic caused predominantly by DENV-2 occurred in the southern part of Taiwan, Kaohsiung area, during 2002, following a previous large outbreak of DENV-1 between 1987 and 1988 in the same area. More than 5000 symptomatic cases of dengue were reported in the 2002 dengue epidemic and a large number of patients were adults.[4,5] Whilst dengue has been studied extensively in children,[6] little is known regarding the clinical differences between children and adults with dengue virus infection, particularly in Taiwan. The aim of this study was to understand better the differences in clinical and laboratory characteristics and disease severity between children and adult patients with the DENV-2 dominant infection in Taiwan in 2002.[5]

2. Materials and methods

A retrospective study of serologically confirmed dengue-infected patients admitted between June and December 2002 to Chang Gung Memorial Hospital-Kaohsiung (CGMH-KS) was conducted. CGMH-KS is a 2500-bed medical facility serving as a primary care and tertiary referral centre in Kaohsiung, Taiwan. The medical records of all included patients were reviewed. Enrolled subjects were grouped by age as either children (age <18 years) or adults (age $\geq$18 years). Quality assurance analyses of diagnostic tests for dengue-infected patients were performed by the Centers for Disease Control in Taiwan based on at least one of the following criteria: (i) a positive RT-PCR result; (ii) a positive ELISA result for specific IgM antibody to the dengue virus in acute phase serum; or (iii) a $\geq$4-fold increase in dengue-specific haemagglutination inhibition (HAI) titres in convalescent serum compared with acute phase serum. Patients diagnosed by a specific IgM antibody ELISA to dengue virus in acute phase serum had to be serologically concomitantly negative for the specific IgM antibody to Japanese encephalitis virus (JEV).[4,5]

The demographic characteristics, initial symptoms/signs and laboratory data [including peripheral white blood cell (WBC) count, haematocrit levels, platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, serum total bilirubin, blood urea nitrogen (BUN), creatinine and albumin levels] of the included patients were obtained from medical charts. The initial symptoms/signs and laboratory data of the included patients were defined as those recorded and assayed upon their arrival at the hospital (via the emergency room or outpatient department). The day of admission was defined as the day when the patient was admitted to CGMH-KS following the onset of the illness (beginning of fever).

Renal insufficiency was defined as (i) elevated serum BUN (>20 mg/dl) and creatinine (>1.4 mg/dl) in a patient with original normal kidney function or (ii) an increase in the baseline serum BUN and creatinine value if a patient had an underlying chronic renal disease after admission to the hospital. Acute renal failure was defined as oliguria with abruptly elevated serum BUN and creatinine after the patient was hospitalised for dengue illness. Liver function impairment was defined as an increased ALT level at least 2-fold higher than the upper limit of normal (ULN) serum ALT level (ULN > 40 U/l). Acute hepatic failure was defined as development of encephalopathy or jaundice, prolonged PT [>3 s compared with that of control (12 s)] and severe liver damage (elevated ALT, >3-fold that of normal value). Chest radiographs were interpreted by an experienced chest physician to obtain information regarding pulmonary lesions or pleural effusion. Abdominal ultrasound was performed by an experienced hepatogastroenterologist to collect information regarding intra-abdominal lesions.

In the serologically confirmed dengue-infected patients, a diagnosis of DHF was made based on WHO criteria, i.e. presence of fever, haemorrhagic phenomena, thrombocytopenia and haemoconcentration ($\geq$20% rise in haematocrit above the baseline value or presence of pleural effusion and/or ascites).[3] DHF cases were further graded as I—IV in severity according to WHO guidelines.[3] Grades I and II DHF were indicated by abrupt onset of fever, thrombocytopenia (<100 000/μl), evidence of plasma leakage (haemoconcentration or signs of serous effusion) and haemorrhagic tendency. A positive tourniquet test result and/or easy bruising in the absence of spontaneous bleeding was assumed to differentiate grade I from grade II DHF. Grade III DHF was diagnosed when the above signs were accompanied by circulatory failure manifested by a rapid and weak pulse and narrowing pulse pressure (<20 mmHg) or hypotension with cold clammy skin and restlessness. Patients with undetectable blood pressure or pulse were diagnosed with grade IV DHF. DHF grades III and IV were collectively classified as DSS.

Data regarding haemorrhage, including petechiae/ecchymoses, haemoarthritis, haematuria, haemoptysis, epistaxis, upper gastrointestinal (UGI) bleeding, and gum, oral, vaginal, conjunctival and retinal bleeding, were obtained from medical records. Acute respiratory failure was defined as follows: immediate intubation with mechanical ventilation support after failed response to 40% oxygen via a nasal cannula as confirmed by (i) hypoxemia [partial pressure of O_2 in arterial blood (PaO_2) <60 mmHg] or hypercapnia [partial pressure of CO_2 in arterial blood ($PaCO_2$) >50 mmHg], (ii) bradypnoea (respiratory rate <10/min) or tachypnoea (respiratory rate >35/min) and (iii) severe chest retraction and nasal flaring.[7] Concomitant bacterial infection was defined as positive bacterial growth from cultures of blood samples after the patient was hospitalised for dengue illness in those who met the diagnostic criteria for dengue infection.

A retrospective analysis was also conducted to compare initial laboratory data between DENV-positive and DENV-negative adult and paediatric patients. The DENV-negative control subjects were sex- and age-matched patients (admitted to internal medicine or paediatric wards)