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ScienceDirect
Acta Tropica 101 (2007) 153–158
ACTA TROPICA
www.elsevier.com/locate/actatropica

Seroprevalence of dengue in Trinidad using rapid test kits: A cord blood survey

C.A. Campbell [a], A. George [b], R.A. Salas [b], S.A. Williams [a], R. Doon [c], D.D. Chadee [d,*]

[a] *Department of Biology, Smith College, Northampton, MA, USA*
[b] *Caribbean Epidemiology Centre, P.O. Box 164, Port of Spain, Trinidad, West Indies*
[c] *Ministry of Health, 63 Park Street, Port of Spain, Trinidad, West Indies*
[d] *Department of Life Science, University of the West Indies, St. Augustine, Trinidad, West Indies*

Received 29 December 2005; received in revised form 2 October 2006; accepted 1 November 2006
Available online 24 January 2007

Abstract

A cross-sectional sero-epidemiological study was conducted to determine the prevalence of dengue in Trinidad. Two commercial rapid test kits, PanBio Dengue Duo IgM and IgG Rapid Strip Test and the Bio-Check Plus Dengue G/M Cassette Test (Brittney) were used. The immunosorbent assay (ELISA) (FOCUS Technologies, California) was used as the control. One hundred and twenty five cord blood samples were collected (46 from Mt. Hope Women's Hospital (MH) and 79 from the San Fernando General Hospital (SF)). All blood samples were tested in accordance with the two rapid kits and ELISA assay manufacturer's instructions.

From 125 cord blood samples, the IgG FOCUS ELISA results showed 93.5 and 95% infections at MH and SF, respectively. Whereas the Brittney and PanBio kits showed 10.9 and 5.1%, and 26.1 and 50.6% for MH and SF, respectively. Based on the FOCUS ELISA (control) assays, the combined seroprevalence rate from north and south Trinidad was 94.4%. IgG and IgM sensitivity and specificity levels were higher in the PanBio than Brittney test kits. The high seroprevalence rates observed in Trinidad are discussed to stimulate more research to explain this phenomenon and to prevent the Southeast Asian scenario from developing in the Americas.
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Keywords: Dengue; Rapid kits; Seroprevalence; Cord blood; Trinidad

1. Introduction

Dengue virus serotypes 1–4 are responsible for a wide spectrum of clinical manifestations, including dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Most dengue infections are asymptomatic, but there has been a dramatic expansion of more severe dengue disease (DHF/DSS) in the past few decades (Gubler and Kuno, 1997). The current dengue pandemic emerged first in Southeast Asia and has subsequently spread throughout the tropical and subtropical areas of the world, including the Americas (Gubler, 1998). Each year there is an estimated 50–100 million cases of DF and about 500,000 cases of DHF worldwide (Keating, 2001). Risk factors for DHF/DSS include presence of the vector, *Aedes aegypti* (L.), the dengue virus strains (Rosen, 1977) and previous infections with a heterologous serotype (Halstead, 1981).

The first confirmed case of DF was reported in Trinidad in 1953 (Anderson et al., 1956), and frequent DF epidemics have occurred in the Caribbean since the

* Corresponding author. Tel.: +1 868 645 3232 7x3740; fax: +1 868 663 5241.
E-mail addresses: Chadee@tstt.net.tt, dchadee@fsa.uwi.tt (D.D. Chadee).

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doi:10.1016/j.actatropica.2006.11.009

1970s. After the 1981 DHF epidemic in Cuba (caused by Southeast Asian genotype Den-2, the first in the Caribbean), epidemics of severe dengue have occurred throughout the region (PAHO, 1979). It is noteworthy that the introduction and co-circulation of multiple serotypes, including the Asian genotypes, along with unplanned urbanization, re-infestation of the mosquito vector *A. aegypti* in previously free countries and frequent air travel have contributed to the emergence of DHF (Rico-Hesse et al., 1997; Chadee and Martinez, 2000; Chadee et al., 2004). Most recently, Den-3 was reintroduced into Central America, causing a severe DHF outbreak in Nicaragua (Guzman et al., 1997), and then endemic transmission in the rest of the Americas. Den-3 has been endemic in Trinidad and Tobago since 2000 (Salas and George, 2002).

Unlike the current situation in Southeast Asia with most DHF/DSS cases in children, in Trinidad and the rest of the Caribbean DHF/DSS affects all age groups (Chadee et al., 2004). The first cases of DHF/DSS in Trinidad were reported in 1992 and 1993 in adults and young adults ages 15–53 (Teelucksingh et al., 1997). Cases have since been reported in Trinidadian children and many fear that the Southeast Asian scenario, in which dengue is a major cause of hospitalization and death among children, will emerge in the Americas (Teelucksingh et al., 1999; Chadee et al., 2004).

A prospective seroepidemiologic study in Thailand found that 87% of infected schoolchildren were asymptomatic or mildly symptomatic (Burke et al., 1988). Because many dengue infections do not produce symptoms, the number of reported cases greatly underestimates actual dengue prevalence. Along with surveillance of suspected dengue cases, serological surveillance of the general population is important in order to monitor the risk of DHF/DSS and to predict and control epidemics. Recently, several commercial kits have become available for the rapid detection of IgM and IgG antibodies to dengue virus in human serum and/or whole blood. It is noteworthy that antibody profiles elicited by primary and secondary dengue infections differ (Innis et al., 1989; Summers et al., 1984). Primary infections result in the initial appearance of detectable DEN-specific immunoglobin M (IgM) antibodies after approximately 5 days of illness, peaking within 2 weeks of illness. Approximately, 3 months after infection DEN-specific IgM antibodies become undetectable (Nogueira et al., 1992). In the acute and early convalescent phase of illness, DEN-specific IgG antibodies appear at low levels and usually remain below IgM antibody levels for 2–4 weeks. During secondary infections, DEN-specific IgM levels remain low to absent in subsequent infections with two or three different serotypes whereas IgG increases rapidly to very high levels and is easily detectable (Porter et al., 1999). A number of studies have been published assessing the sensitivity and specificity of rapid kits for dengue diagnosis with variable results (Groen et al., 2000; Vaughn et al., 1998; Sang et al., 1998; Wu et al., 2000). These assays are intended for diagnosing current infections, but would be very useful if they could be applied to monitoring seroprevalence in the general population in endemic countries because they are inexpensive, require no equipment or training, and can be easily used in the field.

Little or no information exists on dengue seroprevalence in the Caribbean, and to our knowledge no study of dengue seroprevalence has been done previously in Trinidad and Tobago. The goals of this study are twofold: to estimate dengue seroprevalence in the Trinidad population, and to assess the usefulness of two commercial rapid test kits, the PanBio Dengue Duo IgM and IgG Rapid Strip Test (Brisbane, Australia), and the Bio-Check Plus Dengue G/M Cassette Test (Brittney Ltd., Texas), as tools to monitor dengue seroprevalence in the healthy population. The present study is a cross-sectional serological survey of cord blood collected at two hospitals in Trinidad using these two immunochromatographic tests (ICT) and commercial IgM capture and IgG enzyme-linked immunosorbent assays (ELISA) (Focus Technologies, California). Seroprevalence in cord blood is especially important to monitor since the presence of maternal antibodies is a risk factor for DHF/DSS in infants (Kliks et al., 1988).

2. Materials and methods

2.1. Study design and population

A cross-sectional seroepidemiologic survey was conducted to evaluate the performance of two commercial rapid test kits, the Dengue Duo IgM and IgG Rapid Strip Test (PanBio, Brisbane, Australia) and the Bio-Check Plus Dengue G/M Cassette Test (Brittney Ltd., San Antonio, TX, USA). Commercial microplate IgM and IgG enzyme-linked immunosorbent assays (ELISAs) (Focus Technologies, Cypress, CA, USA) were used as the gold standard to evaluate the results from the rapid kits. Cord blood samples that had already been collected for other screening procedures were acquired with permission of the Ministry of Health and the individual institutions. Samples originated from Mount Hope Women's Hospital (MH) in North Trinidad, and San Fernando General Hospital (SF) in South Trinidad. It is a common conception among the Trinidad population that South

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