Seroprevalence of Anti-dengue Virus Antibodies in Children in Colombo District, Sri Lanka

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Abstract

Dengue is a growing public health problem globally, including in Sri Lanka. The severity of dengue infection is influenced by the serotype/genotype of the infecting virus, previous exposure of the patient to dengue virus infections, and the age of the patient. Mild and sub-clinical infections are not reported and many clinical diagnoses are not confirmed by laboratory testing. Hence, there are no clear data concerning the proportion of the Sri Lankan population which is susceptible to infection. To elicit this information, blood samples from 313 children up to the age of 17 years, randomly selected from four schools in Colombo district, with no evidence of a recent dengue infection or a family recollection of a dengue infection, were collected. These were tested for the presence of anti-dengue virus antibodies by indirect ELISA. The study brought out that 34% of the children had evidence of inapparent infection with a flavivirus, most probably dengue virus. The majority of children in Colombo district have not been infected with dengue virus despite the presence of both the virus and the mosquito vectors.

Keywords: DF/DHF, children, subclinical infection, seroconversion, Sri Lanka.

Introduction

During the 19th century, dengue was considered a sporadic disease, causing epidemics at long intervals. However, dramatic changes in this pattern have occurred and currently, dengue ranks as the most important mosquito-borne viral disease in the world. It may give rise to an undifferentiated fever, dengue fever (DF) or dengue haemorrhagic fever (DHF). However, infection may be inapparent, particularly in very young children.

Dengue viral infections have been endemic in Sri Lanka since the mid-1960s when the first cases of DF/DHF were reported. An island-wide seroepidemiological survey, which was carried out in 1966-1967 using the haemagglutination inhibition (HI) test, revealed that DENV activity was endemic throughout the country. However, despite evidence of exposure to the virus in many individuals, major epidemics of DHF were not reported until 1989 when the first major outbreak of DHF occurred. Since then, there have been regular epidemics in Sri Lanka with...
increasing numbers of cases each year. DHF leads to significant morbidity and mortality, especially among children, with the highest incidence seen in the 5-9 years age group in the years 1999 and 2001 (26.9% and 16.15% respectively). The highest case-fatality rate (3.3–5.2%) was seen in children between the ages of 1–4 years.[5]

In Sri Lanka, the highest incidence is reported in the Western province (50.6% in 2004), with the highest incidence in Colombo district. However, the age-stratified seroprevalence rates among Sri Lankan children living in Colombo district, which is currently the most affected by dengue infections, are largely unknown. It is useful to know the age-related seroprevalence rates to determine the prior exposure of the populations and also to determine the annual infection rate. With these objectives, this study was designed to quantify the proportion of children with prior exposure to dengue virus infection in Colombo district.

Materials and methods

Three-five ml blood was collected from 313 children randomly selected from four schools in a municipal council area in Colombo district (Maharagama Medical Officer Health area). The proportion of children from each school who provided blood was similar to the proportion of the study population each school constituted. Informed written consent was obtained from parents of all children who participated in the study. A questionnaire was used to obtain information regarding the child’s medical history. Ethical clearance for the study was obtained from the Ethical Review Committee of the Faculty of Medical Sciences, University of Sri Jayawardanapura.

Blood was centrifuged and serum was separated and stored at 4 °C until serological tests were performed. All sera were tested for the presence of anti-dengue virus IgG antibodies using a commercial ELISA which incorporated all four dengue virus serotypes (PanBio, Australia). The sera were diluted 1 in 100 prior to testing. A strong correlation between this ELISA and the haemagglutination inhibition (HI) test has been reported[6,7] and the sensitivity and specificity of the IgG indirect ELISA kit are reported to be 99.2% and 96.2% respectively.[7,8]

Results

Of the 313 children who participated in the study, 157 (50.1%) were females. The mean age was 13.1 years (SD±3.1). One hundred and seven of the 313 children (34.1%) had IgG antibodies which reacted with at least one dengue virus serotype in an indirect ELISA. None of these children gave a past history of admission to hospital due to a febrile illness and, therefore, it is likely that these children had mild or asymptomatic dengue infections. The seroprevalence rates were not significantly different in females (49.5%) and males (50.4%) (Chi-square test; P>0.05).

No sera were available for children under six years of age, but by this age, approximately 30% had IgG antibodies that recognized the dengue virus. Therefore, this indicates an annual seroconversion rate of 5% per annum for dengue infections in children under six years of age. The percentage of seropositive children in each age group increased with age (Spearmans r value 0.45) (Figure). Between the ages of six and 17 years, the annual seroconversion rate was approximately 1.5% per annum. Sera which reacted with the dengue virus in ELISA were re-tested at doubling dilutions. There was no significant increase in antibody titre with the age of the donor.
Discussion

This study suggested that dengue viral infections were common among schoolchildren in Colombo district and that most were either asymptomatic or mild enough not to require hospital admission. The difference in the rates of infection prior to entering school (approximately 5% per annum) and over the subsequent 11 years (approximately 1.5% per annum) raises the possibility that most infections with dengue viruses are occurring in and around the home, particularly when children are young and relatively less mobile. If this is the case, there is an opportunity for disease prevention education targeted at mothers, perhaps immediately post-natal. Although there is a rare possibility that the dengue-specific IgG antibodies detected by ELISA could be due to cross-reactive antibodies to other flaviviruses present in Sri Lanka, this is highly unlikely due to the sensitivity and specificity of the test used. However, the presence of such cross-reactive antibodies giving rise to false positive results cannot be totally excluded.

The dengue antibody seroprevalence rate in Sri Lanka, estimated in this study, is lower than that reported in some studies in Thailand (71% of primary schoolchildren) and Viet Nam (38% in 4-year-olds rising to 69% in 9-year-olds) but similar to that reported in Singapore (45%). Although we do not know the seroprevalence of anti-dengue antibodies in adults, it is likely to be less than what is seen in India, where 100% adults are seropositive. Furthermore, dengue virus antibody titers did not increase with the age of an individual in our study. This suggests that the children who had dengue virus antibodies in their serum may have been infected only once and with just one serotype of the virus.

It seems remarkable that despite the presence of dengue viruses, mosquito vectors and environmental conditions similar to much of South-East Asia, dengue is not as serious a problem in Sri Lanka as in other countries in the region. The low dengue seroconversion rates measured in this study confirmed that the comparatively lower disease incidence in Sri Lanka was not due to differences in the rates of disease reporting. The explanation may lie in the competence of local mosquitoes to transmit dengue viruses. This should be investigated.*

*In any physical or biological phenomenon the interacting forces are at their maximum at the epicentre (eye of the storm), but get weakened spatially in the diffusion area. Thailand has been considered as the epicentre of DF/DHF where the transmission intensity is at its highest. The interacting factors related to host viruses and mosquito vectors will be at variance in the countries situated in the diffusion areas. The ability of the vector system in recent years has been defined as comprising of two components: (i) vector competence denoting susceptibility of the species to the virus, its replication and the ability of transmission to the new host; and (ii) vectorial capacity being influenced by biological, ecological and environmental factors. Generally, vector competency does not differ in the epicentre and diffusion areas, but vectorial capacity does vary in diffusion areas. – Editor
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References


