Synopsis of Findings from Recent Studies on Dengue in Sri Lanka

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Abstract

The pattern of dengue in Sri Lanka changed after 1989, with an exponential increase in the incidence of DHF. In 2004, a major epidemic of dengue infection occurred in Sri Lanka, which accounted for 15 457 cases and 88 deaths. The findings from recent studies on dengue are outlined here, which highlight the implications with regard to the management and control of this infection in the country.

Keywords: Dengue, adults, children, Sri Lanka.

Introduction

Dengue is the most prevalent mosquito-borne viral infection worldwide. Around 100 million cases of dengue fever (DF) and half a million cases of dengue haemorrhagic fever (DHF) are estimated to occur annually.[1] The pattern of dengue changed in Sri Lanka after 1989, with an exponential increase in the incidence of DHF.[2,3,4,5] Before this, DHF was rare, despite circulation of more than one dengue virus serotype. Subsequently, the pattern of the severe type of disease changed and regular epidemics of DHF have since been reported. Similar trends are also present in some other countries of the Indian subcontinent.

The number of cases of dengue reported and deaths due to dengue in Sri Lanka from 1985 to 2005 are shown in Figure 1 (a, b). The relative proportions of the DENV-1, DENV-2, DENV-3 and DENV-4 serotypes in Sri Lanka between 1989 and 2004 are shown in Figure 2. From 1989 to 2002, DENV-2 was the main circulating dengue serotype in Sri Lanka, followed closely by DENV-3.[2,6,7] However, during the 2004 epidemic, the DENV-3 virus appeared to be the predominant serotype

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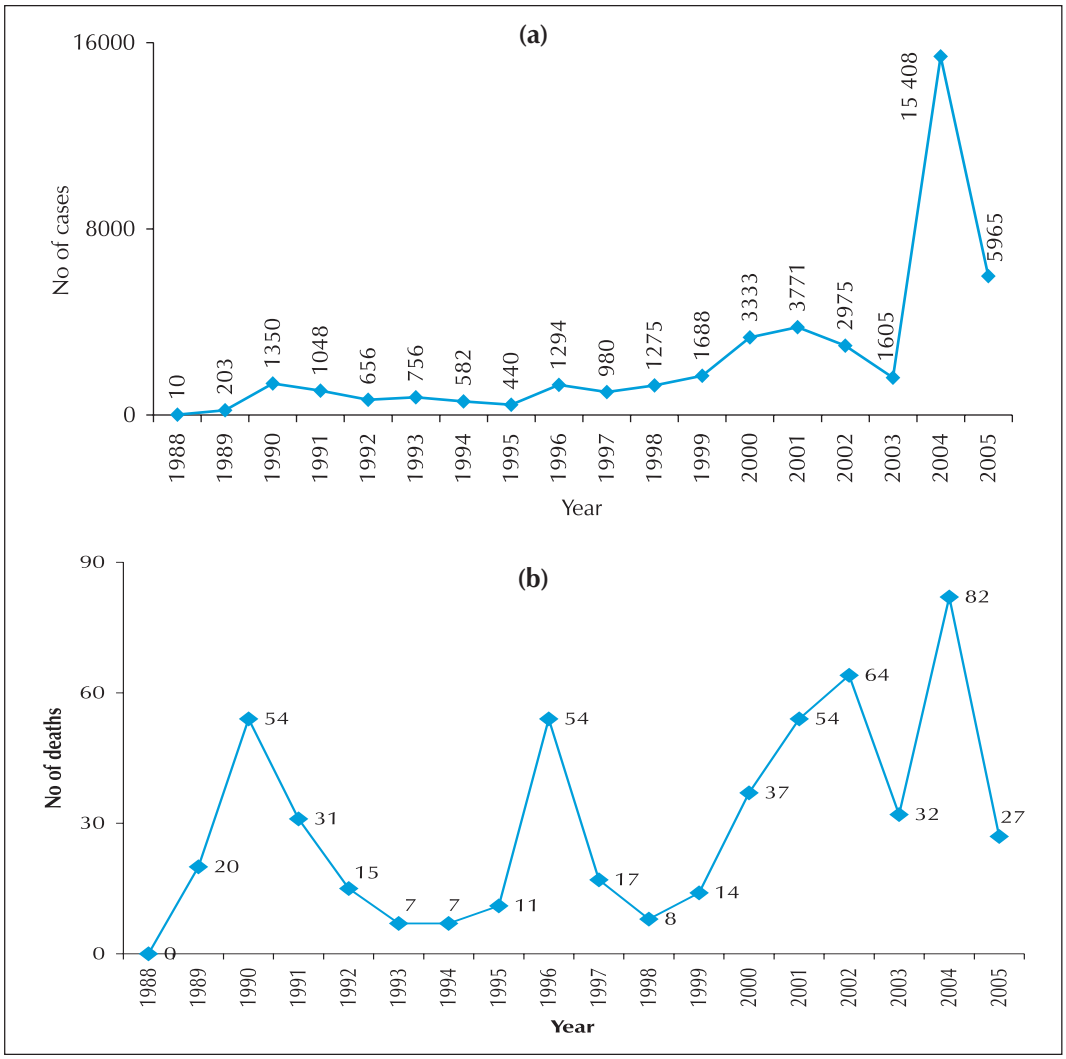
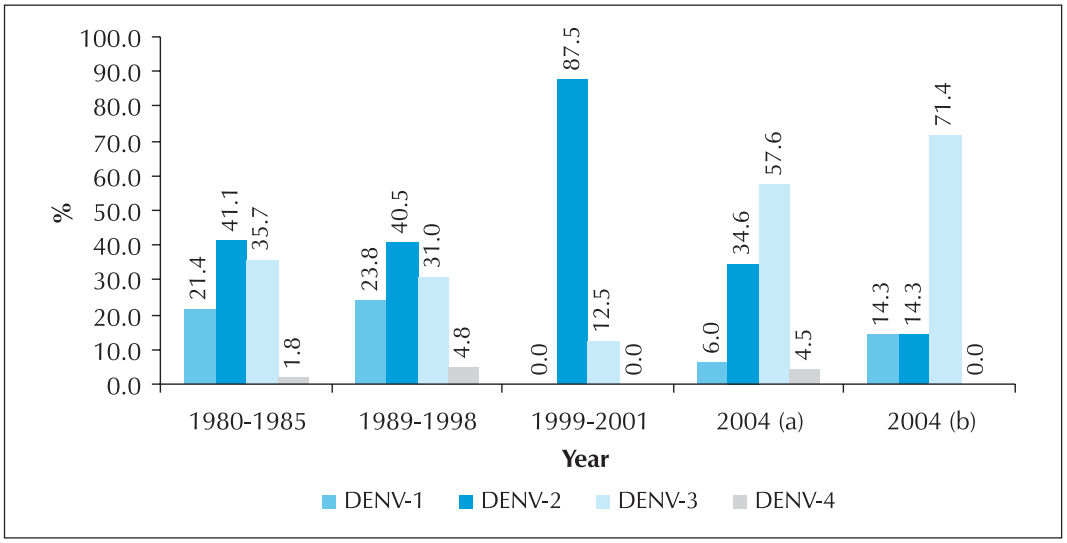
Figure 1: ***(a) Number of cases of dengue reported, and (b) Deaths due to dengue in Sri Lanka from 1985 to 2005***



(Figure 2).[8,9,10] A study suggests that the emergence of DHF in Sri Lanka in 1989 correlated with the appearance of a new DENV-3, subtype III, variant. It has been postulated that mutation of the viral genome led to the emergence of this new variant.[11]

In 2004, a major epidemic of dengue infection occurred in Sri Lanka, which accounted for 15 457 cases and 88 deaths. Although the exact reasons for this epidemic have not been defined, a change in the predominant circulating dengue viral serotype may have played a role. During this epidemic, we studied the clinical and laboratory findings in a group of hospitalized children and adults with dengue [Figure 2 – 2004 (a)].[12,13] In addition, two other studies on dengue in Sri Lanka have been published

Figure 2: ***Relative percentages of dengue serotypes in Sri Lanka between 1989 and 2004***



[Figure 2 – 2004 (b)] recently.[14,15] These different studies provide important insights into the patterns of dengue disease in Sri Lanka and important findings of these studies are summarized below.

Methods

The main findings from recent studies on dengue in Sri Lanka were selected and described and its implications for Sri Lanka and other dengue endemic countries were outlined.

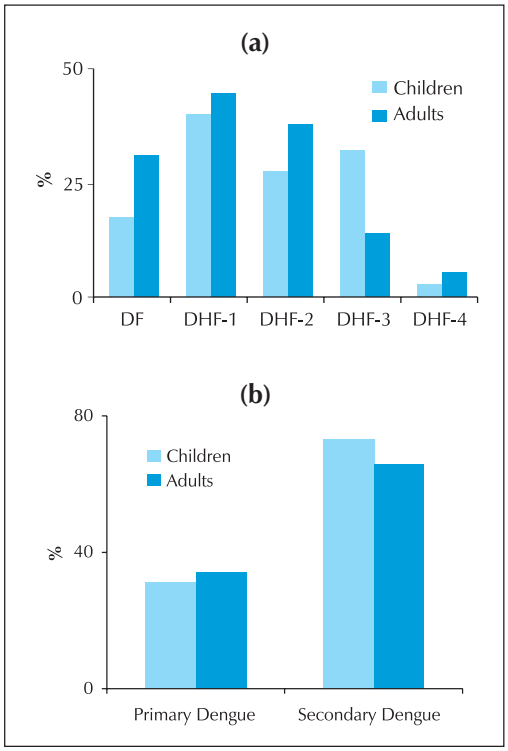
Results

Dengue in hospitalized children

One hundred and four hospitalized children with dengue were studied [43 (40.2%) male, mean age 7.9, SD 2.9 years]. Some characteristics of the disease found in these children are shown in Figure 3. The odds ratio for children with secondary dengue infection to develop DHF was 9.8 (95% CI 3.1-31.2). This is similar to the findings in children from South-East Asia and the Americas.[16,17] One fifth of the children with DHF had a primary infection, which is different from the profile normally described. Oral candidiasis was seen in 18% of the children. This finding was nearly 20 times higher than among other hospitalized sick children seen during the same period. Over 70% of those children who developed oral candidiasis had a body mass index (BMI) for age $<5^{th}$ centile.

There was no significant association between platelet counts, bleeding manifestations and a positive tourniquet test. Over 50% of the children had abnormal liver enzymes [high alanine aminotransaminase (ALT), 49%; high abnormal aspartate transaminase (AST), 67%], with AST levels being significantly higher in children with DHF than with DF as seen in previous reports.[18] A higher incidence of dengue encephalopathy (5.6%) was seen as compared with other reported series.[19] Poor nutritional status was not a risk factor for severe dengue disease in our children.

Figure 3: ***(a) Percentage distribution of DF, DHF-1, 2, 3, 4, (b) primary and secondary dengue in hospitalized children and adults in Sri Lanka***



Dengue in hospitalized adults

One hundred and eight hospitalized adults with dengue [64 (59.3%) males, mean age 26.6 SD 9.9 years] were studied. Some features of the disease in these adults are shown in Figure 3. Secondary dengue infection was significantly associated with the development of severe disease (odds ratio 5.0, 95% CI 1.9-13.5. $P<0.001$). A high proportion of the patients with DHF had abdominal symptoms: diarrhoea (32%), vomiting (68%) and abdominal pain (18.7%). In some patients, the abdominal pain simulated an acute surgical abdomen and highlighted the need for medical personnel suspecting dengue in diverse clinical situations so as to initiate appropriate management.

A descriptive observational study was also conducted in the Central Province of Sri Lanka in 2001, enrolling 404 adults. Patients were categorized into different serology groups and the clinical features noted; which included fever duration (range 1-19 days), headache, myalgia, vomiting, rash and flush. The mean total white blood cell count and platelet count started to fall from the second day of fever with the lowest counts on the 5th to 7th day. A majority of the patients (88%) had elevated liver enzymes. Complications such as myocarditis, effusions, encephalopathy, acute renal failure, acute liver failure and diarrhoea were observed.[14]

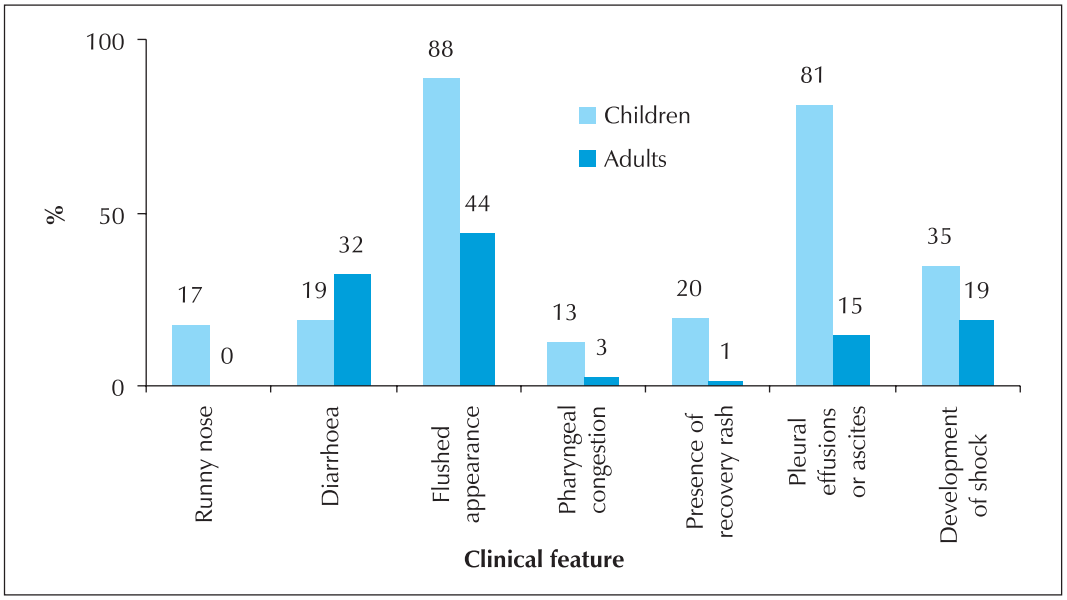
Differences between hospitalized children and adults with dengue

Differences in the clinical findings between children and adults with dengue are shown in Figure 4. No relationship between platelet counts and bleeding manifestations were found in these children. In contrast, a platelet count $<50\times10^9$/l and packed cell volume (PCV) >50 among the adults were significantly associated with the presence of bleeding manifestations.

Changing disease pattern: outbreak of myocarditis

We also observed an outbreak of myocarditis caused by the dengue virus in the Central Province of Sri Lanka in 2005. A total number of 174 patients with dengue fever were admitted to the General Hospital, Peradeniya over a period of two months. The diagnosis was serologically confirmed in 120 patients and, of them, 75 (62.5%) patients had cardiac involvement.[20] Polymerase chain reaction (PCR) testing was done on acute blood samples of 20 patients, and, in three samples, DENV-3 was the causative serotype. None of these patients had DHF and most of those affected were hospital workers and medical students, suggesting a clustering of cases.[20]

Figure 4: ***Differences in clinical findings (%) between hospitalized children and adults with dengue***



Discussion

During the past few years, the characteristics of dengue in Sri Lanka appear to have changed. For instance, a decade ago, children were predominantly affected, but in recent years, clinicians have seen increasing numbers of adult dengue patients, with significant morbidity, and increasing numbers of adult deaths due to dengue.[13,14] Similar trends are seen in some South Asian, South-East Asian and South American countries.

The rise in the incidence of dengue among Sri Lankan adults adversely affects the country's developing economy and also its health planning. The situation has been compounded by the general lack of systematically collected information on the natural history of dengue in Sri Lanka. This lack often leads health planners and clinicians to base their decisions regarding resource allocation and clinical management on personal experiences rather than on tangible evidence. For instance, a survey of the opinions of 50 consultant physicians and paediatricians on the management of dengue found widely varying views and practices by both the groups. The usage of platelet and plasma transfusions was not based on any specific guidelines.[15] This survey clearly highlights the need for formulation of a consensus guidelines suitable for the Sri Lankan setting.[15]

Myocarditis as a sporadic complication of dengue fever has been previously reported.[5,20] However, its emergence as a major outbreak has not yet been described. This again may be related to subtle changes in the infecting viral genome. Clinicians need to look out for these newer manifestations and trends and use these findings to develop appropriate management guidelines and strategies.

Dengue has significant adverse financial effects in several countries. For example, in Thailand, the financial loss due to dengue has been estimated at about US$ 61 per family, a

value that exceeds the average monthly income.[21] Although the economic impact of dengue infections has not been formally assessed in South Asian countries, it is likely to be of similar magnitude as in Thailand.

A sizeable proportion of children hospitalized with dengue infection seen by us developed oral candidiasis. Although the reasons for this manifestation have been postulated,[12] specific studies to dissect each case were not done. Studying the underlying reasons for this manifestation during future dengue epidemics may provide useful leads in understanding the overall dengue pathogenesis. Although nearly 40% of adults in our cohort had a primary dengue infection, quite severe clinical manifestations were noted in a significant proportion of the patients. Possible reasons could include a non-immune adult population being exposed to a more virulent viral serotype, or these individuals might have had simultaneous infection with one or more dengue viruses.

Conclusions

Dengue infections are now well-established in Sri Lanka. The prevailing climatic conditions, environmental pollution, rapid urbanization, over-crowding of cities and careless human practices are proving conducive for the rapid breeding of the mosquito vector and the spread of this infection. The Ministry of Health has launched preventive dengue programmes and established a special unit for dengue control. In recent times, clinicians and researchers with special interests in dengue have been studying different aspects of this disease. Findings from these studies have been outlined in this review and their implications have been discussed. Comparative studies from different countries should help clinicians and health administrators make more informed and evidence-based health-planning decisions, and also enable them to use pooled data from several countries to study the disease trends and variations.

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