Dengue in Latin America – A Unique Situation

by

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Abstract

The incidence and distribution of dengue virus infection in the tropical regions of Central and South America, as well as the Caribbean, has dramatically increased during the last two decades as a consequence, among other factors, of a wider distribution of *Aedes aegypti*, higher population density in many large urban areas, lack of effective programmes to contain vector development and deterioration of the urban environment. Some distinctive epidemiological patterns of transmission, such as the occurrence of large epidemics of both dengue fever and dengue haemorrhagic fever separated by long periods of absence of viral circulation among the population, are seen in the area. Concurrent circulation of all four serotypes of the virus is not unusual, favouring the occurrence of more cases of secondary infections, and a higher risk of dengue haemorrhagic fever and dengue shock syndrome. Unlike other geographic regions, in the Americas older age groups are widely involved. Some clinical manifestations of dengue in adults appear to differ from those habitually described in children and unusual complications, such as acute acalculous cholecystitis and parotitis, have been described. Further clinical information needs to be generated on the impact of dengue virus co-infection with other endemic agents present in the area.

Keywords: DF/DHF, *Aedes aegypti*, deterioration, urban environment, acute acalculous cholecystitis, parotitis, Americas.

Overview

Although known to cause large outbreaks in the Caribbean since the first half of the 17th century, and continental epidemics or true pandemics during the 19th and 20th centuries, dengue virus was isolated for the first time in the Americas in 1953(1,2). The first large epidemic of dengue haemorrhagic fever (DHF) in the region occurred in Cuba in 1981, with 24,000 cases of DHF and 10,000 cases of dengue shock syndrome (DSS) and 158 deaths reported during a 3-month period(1,2,3,4). In 1986 and 1987 massive outbreaks of dengue fever (DF) were reported in Brazil(5,6). Subsequent serological investigations in the same country estimated almost 4 million cases of DF compared with the clinically estimated 1 million(6). In 1988, an outbreak of DF was reported at 1700 m above sea level in Guerrero State, Mexico(7). In 1990, almost one-fourth of the 300,000 population of Iquitos, Peru, contracted DF(8).

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and in the same year, 3,108 cases of DHF with 78 deaths were reported in Venezuela\(^\text{9}\). The last available regional figures, corresponding to the year 2001, indicate the occurrence of 610,625 clinical cases, 15,376 of which were of DHF/DSS, with 92 deaths. Several Latin American countries report the concurrent circulation of all four serotypes of the virus\(^\text{1}\).

During the last decade, the spread of dengue fever was most dramatic in virtually all Latin American and Caribbean countries infested with *Aedes aegypti*. A sharp upward trend in the number of cases reported each year, from over 250,000 in the early 1990s to more than 600,000 by the end of the century, has been observed\(^\text{2}\). Furthermore, serological surveys suggest the occurrence of millions of such infections\(^\text{10}\). In the period between 1968 and 1980, only 60 cases of DHF from five countries, were reported in the entire region. However, after its emergence in Cuba in 1981\(^\text{11}\), epidemics or sporadic cases of dengue haemorrhagic fever (DHF) have been reported in at least 25 countries in the Americas\(^\text{12}\). Since 1989, when a large epidemic with 2,500 cases of DHF occurred, Venezuela has reported large numbers of DHF cases every year, and in 1995 the country recorded the largest regional outbreak with almost 30,000 dengue cases and 5,000 DHF cases. Although DEN-1, DEN-2 AND DEN-4 were isolated during this epidemic, DEN-2 was by large the most predominant serotype\(^\text{13}\).

**Regional epidemiology**

Today, dengue and sometimes haemorrhagic dengue affects most of the American continent and several islands of the Caribbean. According to the Pan American Health Organization (PAHO), dengue transmission has increased significantly in the region in the last two decades (Figure\(^\text{1,4,14}\)).

Overall, between 1995 and 1997, the region experienced an annual increase in DF incidence rate of +12% and +35%, respectively, with a simultaneous increase in the DHF incidence rate of +61.87\%\(^\text{1,14,15}\).
By the year 2000, 27 countries of Central and South America, and the Caribbean, reported dengue transmission, of them, 17 registered cases of haemorrhagic dengue and 10 registered deaths by DHF. The most affected subregion was South America, and the hardest hit countries were Brazil, Ecuador, Colombia, Paraguay and Venezuela.

Major determinants for the occurrence of dengue in Latin America have been defined as follows:[5,7,8]:

**Population growth**

The percentage of urban population and the expansion of mega cities (10 million inhabitants or more) are on the increase. It has been estimated that by 2020, urban population in Latin America will be about 80% of the total (from 42% in 1954), and by 2030, close to 50% of the population will live in mega cities[9,15]. High population provides an opportunity for increased rates of dengue transmission.

**Unplanned urbanization**

Unplanned urbanization is almost always accompanied by lack of civic amenities, inadequate and intermittent water supplies and poor solid waste disposal, and provides increased breeding sites for vector species.

**Air travel**

Globalization of world economies and tourism have promoted increased travel for the people of the region to different parts of the world, including dengue endemic countries. This has facilitated importation of DEN viruses into the region. Importation of south-east Asian strains of DEN-2 and Sri Lankan/Indian strain of DEN-3 are the classic examples. This virulent strain has been responsible for the higher number of DHF cases in the region.

**Poor sanitary conditions**

As in other parts of the world, the main factors directly or indirectly influencing the magnitude of dengue transmission in Latin America appears to be the low socioeconomic levels of the population and poor sanitary conditions[2,11,12]. This has helped in the wider spread of *Aedes aegypti*.

**Deterioration of the public health infrastructure**

Deficient regional public health systems, as well as an ineffectual and obsolete sanitary legislation, are hardly a match to the emergent DHF threat. Besides, due to economic constraints, health authorities are more inclined to take emergency contingency measures rather than undertake preventive activities on a regular basis.

**Is clinical expression of the disease in the region any different?**

In contrast with observations in Asian countries, where DHF is almost completely restricted to young children, in the Americas, older age groups are widely involved[2,6,16,27]. For example, during the Venezuelan outbreak of 1989, about one-third of the deaths were among patients over 14 years of
age, while in the 1997 Cuban outbreak, all of the deaths were among adults\textsuperscript{(19)}. Moreover, in Puerto Rico, in 1990-91, the reported mean age of the patients was 38 years\textsuperscript{(20)}, and during the 1981 Cuban outbreak of DHF/DSS, the frequency of DHF/DSS was higher among female adults\textsuperscript{(19)}. Of late, an increase in the percentage of DHF cases in individuals over 15 years of age has been noticed in Malaysia and the Philippines in recent years\textsuperscript{(28)}; however, young children continue to be the age group predominantly affected\textsuperscript{(26,28)}.

Many potential factors may influence the type and severity of the disease arising out of any epidemic of dengue\textsuperscript{(20)}. The host immune response appears to be a major factor. Sequential infection with different dengue viral serotypes in the presence of non-neutralizing antibodies has been strongly incriminated in the occurrence of DHF/DSS\textsuperscript{(19,20,21)}, and cases of DHF/DSS are seldom documented in patients with primary infection\textsuperscript{(22,23,24,25)}. Besides virus strain virulence, individual factors, such as age, sex, genetic background and underlying diseases, may also play a role\textsuperscript{(19,21,22,25)}.

The severity of the dengue virus infection appears to be influenced by race. For instance, white individuals in Cuba were affected more significantly than blacks and mulattos by DHF/DSS in both the recent outbreaks\textsuperscript{(15,16,19)}. Unlike most Latin American countries, Cuba has a predominance of whites, blacks and mulattos in its population, and lack Amerindians or mestizos, since the native population was completely exterminated during the colonial time.

As epidemics progress, some Latin American countries have recorded a significant steady increase in the proportion of total cases presenting as DHF or DHF/DSS, and in the case fatality rates for both DF and DHF/DSS\textsuperscript{(29)}. Such increases have been explained by the fact that a part of the population with antibodies against a dengue virus serotype raised after natural prior primary infections would react with "neutralization" determinants found on a different serotype. These heterotypic antibodies would not prevent a secondary dengue infection, but would serve to down-regulate the disease to mild illness or symptomless infection. Nevertheless, a sub-population of the new viral serotype that replicates in the hosts immune to the preceding serotype might escape heterotypic neutralization. When inoculated into a new host immune to the prior serotype, these viruses would be free to interact with the more abundant infection-enhancing antibodies, thus producing severe disease\textsuperscript{(29)}.

Adults seem less likely than children to suffer from DSS. Indeed, in a retrospective study of 108 adult Malaysians with DHF, the overall morbidity was significant (29.4%) but the case fatality rate remained low (2.0%). The lowest platelet level occurred on day 6 of the fever. Hyponatremia was observed in 46.8% of the cases\textsuperscript{(30)}.

Some clinical manifestations of dengue in adults appear to differ from those usually described in children. For instance, several comparative studies have found hepatomegaly in only 10.5% of adults, as compared to more than 70% in children\textsuperscript{(31,32)}. 
Unlike children, adults with DHF/DSS often exhibit massive gastrointestinal or other sites bleeding, severe enough to cause death, prior to the onset of shock \(^{32,33}\). In fact, the latter is frequently a consequence of massive bleeding. Liver necrosis may be severe and has been observed in fatal cases among children and adults, both in primary and in secondary infections \(^{20,21,34,35}\).

Of note here is that about 10% of 97 Venezuelan adults with dengue recently studied by us (Torres JR et al. unpublished data) developed acute acalculous cholecystitis (AAC), according to clinical and ultrasonographic criteria. The latter included: enlarged gall-bladder with thickened wall (≥6 mm) and pericholecystic fluid appearing as a halo, tenderness to palpation with the ultrasound probe, or the presence of a diffuse, homogeneous, non-shadowing, medium-level echogenicity within the gall-bladder lumen, were all considered ‘positive’ findings \(^{36}\). Whereas AAC patients exhibited a statistically significant increase in the level of peripheral blood leukocytes, clinical outcome appears not to differ from that of patients without AAC in terms of length of clinical interval prior to admission and hospitalization, or the occurrence of other life-threatening complications. Details of our findings on this newly recognized condition will be discussed elsewhere.

Only scattered reports exist in the medical literature on the pathological and clinical implications of AAC complicating adults with DHF \(^{37,38,39,40}\). However, recent data in children with DHF suggest that a gall-bladder wall thickening ≥5 mm on ultrasonography correlates with a higher risk of hypovolemic shock.

The relatively common occurrence of dengue virus infection among adults in the region allows for the recognition of some complications of the disease harder to be noticed in affected children. This is the case of the recent description by us of acute bilateral parotitis \(^{40}\). Moreover, clinical experience continues to accumulate on the impact of coinfection with dengue virus and other endemic agents present in the area, such as *Paracoccidioides brasiliensis*, *Histoplasma capsulatum*, *Leishmania spp*, etc. \(^{2}\).

In conclusion, DHF/DSS continues to occur in the Americas in a significant number of adults, but it is not clear whether this relates with the genetic background of the populations, epidemiological events, or else, with other unknown factors.

**Regional health impact and perspectives for control**

Little information exists on the impact of dengue in the region in terms of the disease burden. Based on the experience in Puerto Rico, using disability-adjusted life years (DALYs) as a means of assessing the economic impact of dengue, dengue was found to cause the loss of an average of 658 DALYs per year per million population \(^{41}\). It has been estimated that the loss to dengue is similar to the losses per million population in the Latin American and Caribbean region attributed to any of the following diseases or disease clusters: the childhood cluster (polio, measles, pertussis, diphtheria, tetanus), meningitis, hepatitis, or malaria. The loss is also of the same magnitude as any one of the following: tuberculosis, sexually transmitted diseases (excluding human
immunodeficiency virus), tropical cluster (e.g. Chagas’ disease, leishmaniasis), or intestinal helminths. These results suggest that when resources for research and control are allocated regionally, dengue should be given a priority equal to many other infectious diseases that are generally considered more important.

The application of vector control methods, including source reduction, use of chemical larvicides and adulticides and of biological control agents, is hampered by weak programme capacity, the absence of well-defined indicators and programme targets, and poor understanding of the efficacy and cost-effectiveness of control measures, particularly in terms of reducing transmission. Major epidemiological and operational research challenges are a better understanding of the virus transmission dynamics and the identification of transmission thresholds.

A key factor to be considered in any control programme requiring a strong social participation component is “behaviour change”. As in other parts of the world, recent dengue prevention and control programmes in the Americas have relied upon educational approaches, on the premise that knowledge would lead to behaviour change. However, experience with this and similar programmes, such as HIV and diarrhoeal diseases prevention and control, have demonstrated that a poor correlation exists between knowledge improvement and behaviour change. Hence, emphasis must be shifted to the development of behaviour change interventions. For this purpose, ministries of health and communities need to develop stronger links both among themselves and with other key partners in order to achieve a sustainable reduction in the risk of infection and burden of disease.

PAHO reported that in 1995, only about US$ 104,000,000 were spent on dengue control activities in the Americas. This amount is clearly insufficient for the purpose. Therefore, unless significantly larger resources are allocated and more aggressive and effective vector control measures are carried out, the countries of the region will continue to face repeated epidemics of dengue, and, as a consequence, an increased danger of DHF epidemics.

References


