

Dengue—Old Disease, New Challenges in an Ageing Population

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Singapore has experienced yet another epidemic. With more than 13,000 cases reported as of mid July 2013, this could possibly be one of the worst outbreaks in Singapore's history. Dengue claimed its first death in May this year and since then, 4 others have died of dengue. Of these 5 deaths, 80% occurred in patients older than 60 years. The last epidemic from 2004 to 2005 saw more than 14,000 cases with 27 reported deaths. The median age of death cases then was 59.5 years.¹

Mankind has been living with the dengue disease from as early as the Jin Dynasty (265–420 AD) period when the first case of probable dengue was recorded in a Chinese medical encyclopedia.² In the last 50 years or so, we have witnessed an unprecedented expansion in the geographic distribution of epidemic dengue globally. This expansion is facilitated by unplanned and rapid urbanisation in many tropical and subtropical countries, modern trans-national transportation, lack of effective mosquito control and globalisation at a rate that we have not experienced before. Dengue is currently considered by the World Health Organization (WHO) to be one of the most important infectious diseases affecting tropical urban areas in the 21st century. The latest estimate is

that nearly 400 million people are infected with dengue each year with a quarter of these presenting with acute illness.³

Besides the geographic expansion of dengue, the epidemiology of dengue has also been changing. The modal age of disease presentation has also been increasing over the more recent decades. When epidemic dengue emerged in Southeast Asia after the Second World War, it was predominantly a paediatric disease.⁴ However, since the 1980s, there has been an increasing incidence of dengue reported among adults from many parts of the tropics and subtropical countries. Multiple factors have contributed to this trend. In Singapore, the increase in age of dengue cases is likely to be caused by the reduced vector population and hence transmission intensity.^{5,6} Rural to urban migration of adults seeking employment and other economic activity has also raised the age of the population susceptible to dengue infection. At the same time, the world's population is rapidly ageing. Between 2000 and 2050, the proportion of the world's population over 60 years will double from about 11% to 22% with the absolute number expected to increase from 605 million to 2 billion over the same period.⁷ According to Singapore's statistics, by 2050, 38% of our

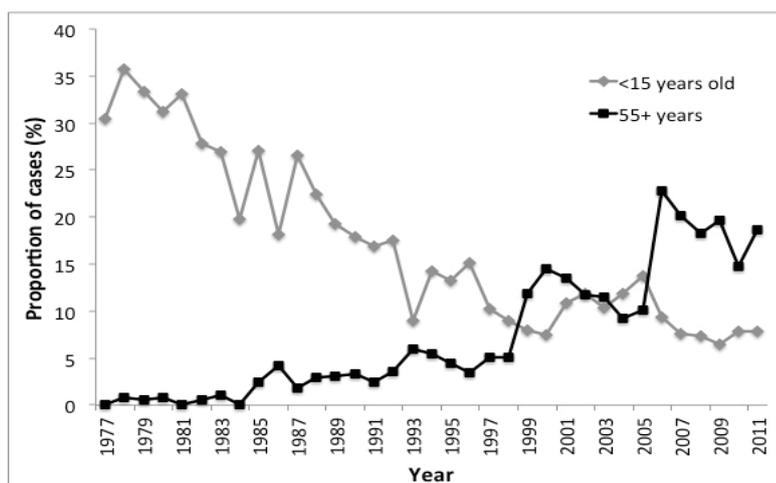


Fig. 1. Proportion of dengue cases in Singapore who are either less than 15 years old or 55 years old and above, from 1977 to 2011. Data obtained from the Communicable Diseases Surveillance in Singapore, published annually by the Ministry of Health, Singapore.

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population will be aged over 60 years.

Dengue in older adults presents fresh challenges. Since the early 1980s, several studies in both Latin America and Southeast Asia have reported a higher association of hospitalisation rates and severe dengue with older ages. The earliest studies were by Guzmán in 1981 in Cuba⁸ and Rigau-Pérez in Puerto Rico.⁹ Subsequent observations were noted in Nicaragua, Brazil and some Southeast Asian countries where dengue transmission has been at epidemic levels for several years.

In Singapore, the age of the reported dengue cases has increased steadily over the last 4 decades (Fig. 1). The proportion of cases below 15 years of age decreased linearly from 30% in 1977 to 7% in 2011. In parallel, the incidence of dengue among the age group ≥ 55 years has been steadily increasing from 0 to approximately 19% in the same period.

With increasing age of the cases, several problems arise. Firstly, the dengue literature mainly describes management of dengue in the paediatric population. Few papers are devoted to optimising management in the elderly. Consequently, the management of elderly with dengue is not evidence-based. Certainly, management protocols have not been critically evaluated in a controlled clinical trial setting. Moreover, the main complication of dengue in children is plasma leakage. This is thought to be mediated by leaky capillaries associated with a growing child.¹⁰ The mainstay of case management for paediatric dengue is meticulous attention to fluid replacement. Adults are less likely to leak plasma.¹¹ Consequently, fluid replacement therapy that is not carefully titrated or monitored could result in fluid overload, particularly if these individuals have pre-existing or undiagnosed cardiovascular disease.

Secondly, clinical recognition of dengue becomes more difficult with increasing age of cases. In a 5-year prospective early dengue infection and outcome (EDEN) study conducted here in Singapore, we showed that the sensitivity of either the 1997 or 2009 WHO dengue classification scheme for clinical diagnosis of dengue reduces significantly with increasing age.¹² In particular, classical symptoms of dengue, such as arthralgia, myalgia, headache and retro-orbital pain were less frequently reported with increasing age of the cases.¹² Likewise, another prospective study conducted in the Emergency Department in Southern Taiwan also observed more elderly patients with isolated fever. Fewer elderly patients had typical presentations of dengue, including symptoms like maculopapular rash. The inability to distinguish dengue from other aetiology of febrile illness early could impede timely hospitalisation or intervention.

Thirdly, the rate of comorbidities increases with age. Some of these have been shown to complicate dengue and increases the risk of severe disease. Pang and others analysed

dengue patients admitted to Tan Tock Seng Hospital between 2006 and 2008 and identified diabetes and hypertension as independent risk factors for severe dengue.¹³ In the EDEN cohort, over half of the patients aged 56 years and above had known comorbidities at the time of admission for dengue.¹² Among them, nearly 45% had hypertension.¹²

Dengue in patients with hypertension may raise another possible outcome: haemorrhagic stroke. The thrombocytopaenia induced during dengue infection is known to increase the risk of internal haemorrhage although the literature often describes this as gastrointestinal bleeds. In the elderly, however, haemorrhagic stroke could be a concern. In reviewing the fatal cases from Tan Tock Seng Hospital in 2004, Ong and colleagues showed that of the 7 fatal dengue cases, 1 had haemorrhagic stroke.¹⁴ This risk is also being recognised elsewhere.¹⁵ Not only does this add to the dengue burden, it could present significant problems in those dengue endemic countries, including Singapore, that have instituted cadaveric transplantation. Organs from deceased who may have died from acute stroke or other cerebrovascular complications may contain dengue virus that when given to the immunosuppressed, could result in catastrophic results.

These problems collectively make dengue diagnosis, triaging for intensive support and case management decisions, challenging. A study examining dengue deaths in Singapore over a 5-year period showed that the median age was 59 years old.¹⁶ Commonest presenting symptoms were fever and lethargy, without the other symptoms suggestive of dengue. Majority did not have any warning signs. Comorbidities existed in 75% of the death cases.¹⁶ In the current outbreak, atypical presentation was also reported in the 4 elderly cases who died during this current outbreak. One patient had main complaints of fever and cellulitis, another patient had fever with hypotension, while another elderly man had mainly gastrointestinal symptoms of fever, vomiting and diarrhoea. The most recent death in a 66-year-old patient presented to the emergency department following a fall at home.¹⁷

In conclusion, as the population ageing trend continues relentlessly, we should anticipate more adult dengue infections and increasing number of elderly diagnosed with dengue. How these trends impact the clinical epidemiology of dengue in the long term, and how this shift in age presentation may affect clinical diagnosis, triaging and management including hospitalisation rate remain to be seen. Nonetheless, studies that clarify management strategies and improve outcome of dengue in the elderly are urgently needed.

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