

CHILDHOOD DENGUE DISEASES: A TWENTY YEARS PROSPECTIVE STUDY

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Abstract. Dengue patients admitted to Department of Pediatrics, King Chulalongkorn Memorial Hospital, Thailand during the period of 20 years from 1987-2007 were prospectively studied. All patients were confirmed as having dengue infection by serology and/or virus isolation. The disease was seen all year round with higher incidence during the rainy season. A progressively increase in the number of cases in adolescent age group were seen. For all age groups, fever, anorexia, nausea and vomiting were most common. However seizures, upper respiratory symptoms and diarrhea were more common in children aged less than 1 year. All severity of dengue diseases can be seen in all age groups. Serologically, both primary and secondary dengue infection can be seen in all age groups while primary dengue infection was more common in children aged less than 1 year. The study emphasizes a significant variation of clinical manifestations of dengue diseases in different age groups, suggesting that a successful management must take into account the different age-specific clinical manifestations since early recognition of the disease is one of the key factors for successful treatment.

Keywords: dengue, children, age, clinical manifestations

INTRODUCTION

Dengue, a rapid growing health problem across the globe is the most common arboviral infection of humans transmitted by *Aedes* mosquitoes, principally *Aedes aegypti*. There are four antigenically distinct, closely related serotypes of dengue virus (DEN 1-4), which belong to the genus *Flavivirus* in the family *Flaviviridae*. A continuum of dengue disease include dengue fever (DF) which causes fever, rash, muscle or joint pain, headache and eye pain; dengue hemorrhagic fever (DHF) causes abnormal hemostasis and increased vascular permeability, with severe cases leading to dengue shock syndrome (DSS). The most common hematological findings include vasculopathy, coagulopathy, and thrombocytopenia. Specific antiviral medications are not available for dengue and successful treat-

ment, which is mainly supportive, depends on early recognition of the disease and careful monitoring for shock (Thisyakorn and Thisyakorn, 2015a). In 2009, the World Health Organization has developed a severity-based revised dengue classification for medical interventions, which has been used in most countries (WHO, 2009).

There is significant variance of clinical manifestations and severity of dengue infection in different age groups such as DF, which have been known in Asia for more than a century are largely age dependent; the disease is mild in children and more severe in adults. Infants and children with DF have symptoms ranging from an undifferentiated fever to a mild febrile illness, sometimes associated with a rash. Older children and adults frequently suffer a more severe form with high fever, pain in various parts of the body, and a maculopapular rash. The infection is only rarely fatal. DSS is more common in children than in adults. Infants with dengue infection present more frequently with convulsions, diarrhea, rash, cyanosis, and splenomegaly while co-morbidities in adults such as peptic ulcers

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disease, preexisting liver disease, which are more likely to be present in adults than in children, can aggravate the disease severity. Thus, proper management of dengue patients must take into account the different age-specific clinical manifestations and severity of dengue disease (Panpitpat *et al*, 2007; Tantawichien, 2015).

Because dengue poses a heavy economic cost to the health system and society, with no specific antiviral medications and successful treatment, which is mainly symptomatic and supportive, depends on early recognition of the disease and careful monitoring for shock. This study aimed at identifying the most prominent clinical manifestations in dengue patients in different age groups in children.

MATERIALS AND METHODS

Clinical data of pediatric dengue patients admitted to King Chulalongkorn Memorial

Hospital, Thailand during the period of 20 years from 1987- 2007 were studied. All patients were seen by one or both of the authors and confirmed as having dengue infection by serology and/or virus isolation. The patients were classified into 4 different age groups: 0-1 years, 2-5 years, 6-9 years, 10-15 years. Comparisons of clinical data in different age groups were analyzed. Variables were compared using chi-square test. The level of significant difference was set at a p -value <0.05 .

RESULTS

A total of 2,090 patients were admitted to King Chulalongkorn Memorial Hospital, a tertiary care hospital in Bangkok, Thailand during 1987 to 2007 with equal number of male and female. One hundred and sixteen cases of which were in the 0-1 year age group (5.6%), 389 cases in the 2-5 years age group (18.6%), 684 cases in the 6-9 years age group (32.7%) and 901 cases in the 10-15 years age group (43.1%) (Fig 1). The disease

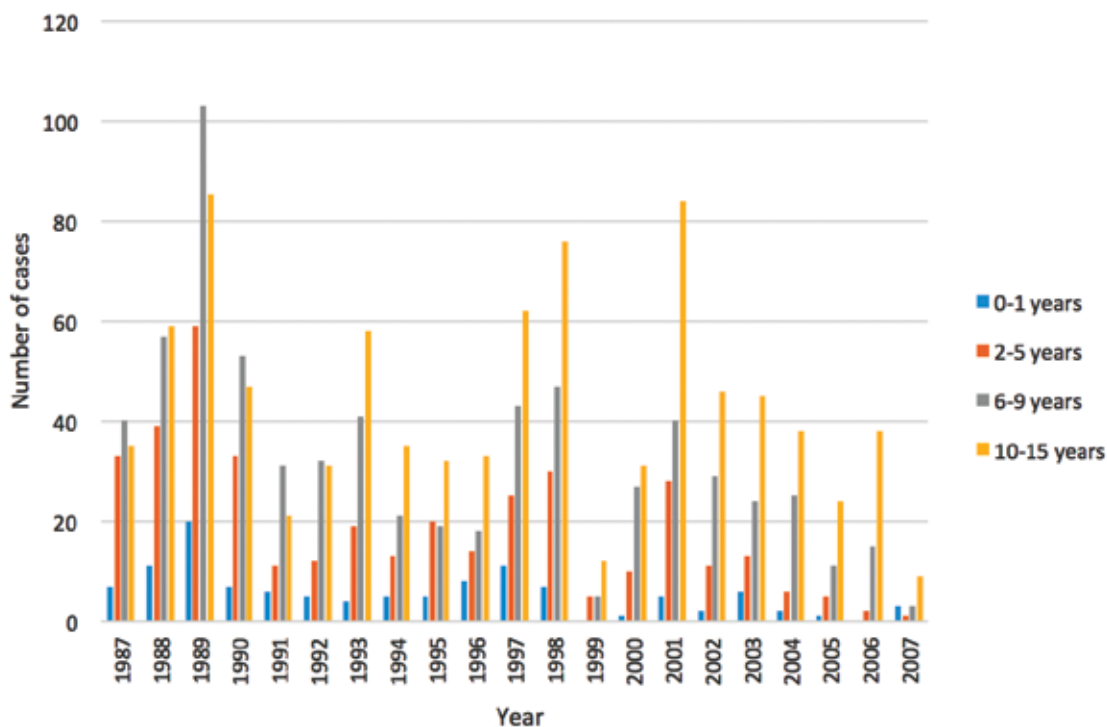


Fig 1—Age distribution of dengue patients in King Chulalongkorn Memorial Hospital between 1987 and 2007.

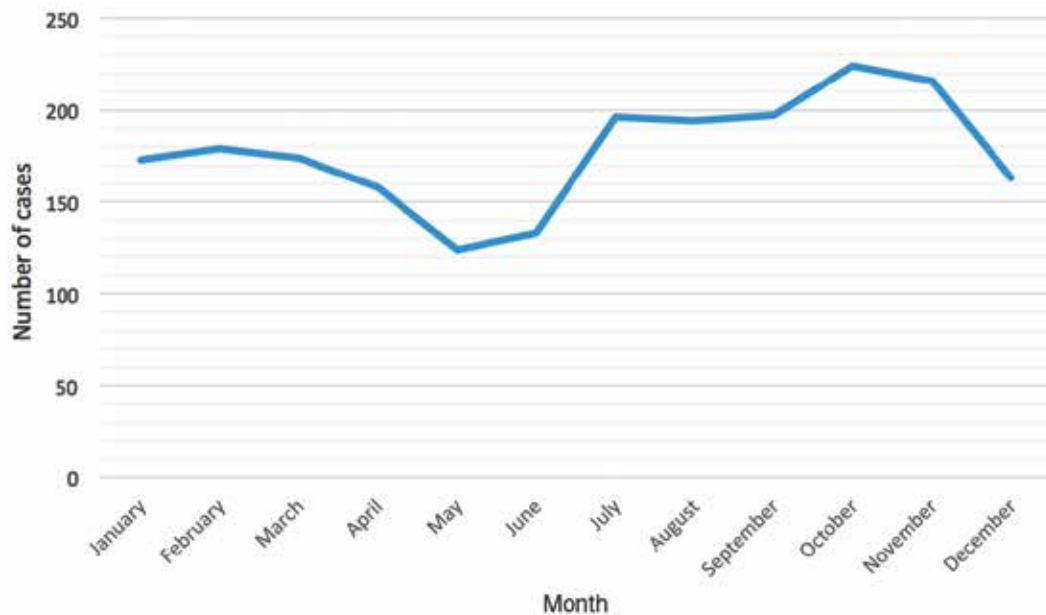


Fig 2–Seasonal distribution of dengue patients in King Chulalongkorn Memorial Hospital between 1987 and 2007.

Table 1. Clinical manifestations of dengue patients in King Chulalongkorn Memorial Hospital between 1987 and 2007.

Clinical manifestation	0-1 years (n=116)	2-5 years (n=389)	6-9 years (n= 684)	10-15 years (n=901)
	n (%)	n (%)	n (%)	n (%)
Fever	116 (100)	389 (100)	684 (100)	901 (100)
Injected conjunctiva	6 (5.17)	35 (9.00)	50 (7.31)	68 (7.55)
Respiratory symptoms	65 (56.03)	186 (47.81)	274 (40.06)	329 (36.51)
Vomiting	51 (43.97)	263 (67.61)	497 (72.66)	635 (70.48)
Abdominal pain	8 (6.90)	167 (42.93)	324 (47.37)	394 (43.73)
Diarrhea	47 (40.52)	68 (17.48)	121 (17.69)	184 (20.42)
Seizures	29 (25.00)	16 (4.11)	9 (1.32)	4 (0.44)
Bleeding	29 (25.00)	96 (24.68)	228 (33.33)	302 (33.52)
Hepatomegaly	98 (84.48)	316 (81.23)	566 (82.75)	619 (68.70)
Splenomegaly	7 (6.03)	5 (1.29)	5 (0.73)	9 (1.00)

was seen all year round with higher incidence during the rainy season from June to October (Fig 2). For all age groups, fever, nausea, anorexia

and vomiting were most common. Abdominal pain and vomiting were more common in older children ($p < 0.05$). However seizures, upper

respiratory symptoms, diarrhea, hepatomegaly and splenomegaly were more common in children aged less than 1 year ($p < 0.05$). Common bleeding sites in all age groups were skin, mucosa, gastrointestinal tract while hypermenorrhea was common in older children (Table 1). All severity of dengue diseases can be seen in all age groups

with overall mortality rate of 0.3% (Fig 3). Serologically, both primary and secondary dengue infection can be seen in all age groups while primary dengue infection was more common in children aged less than 1 year (Fig 4). All severity of dengue diseases can be seen in both primary and secondary dengue infection (Fig 5).

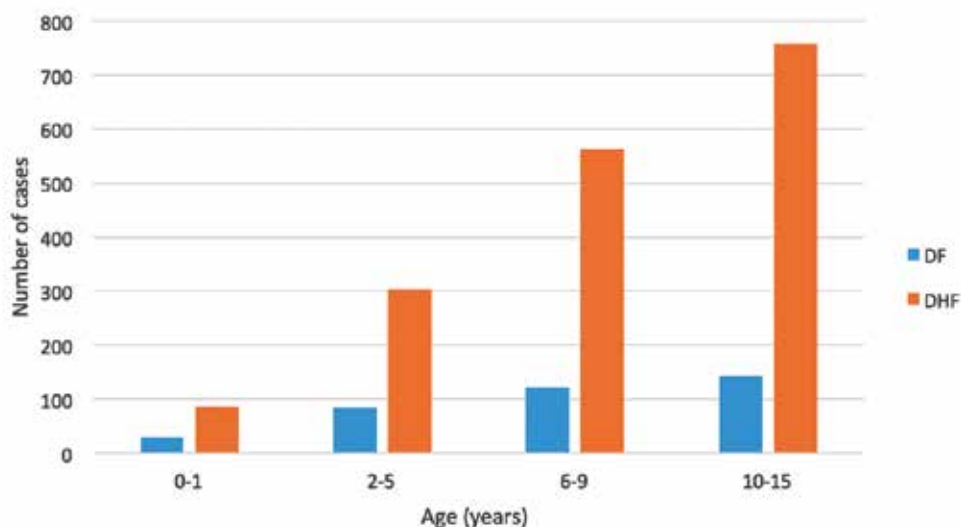


Fig 3—Severity of dengue patients at King Chulalongkorn Memorial Hospital between 1987 and 2007.

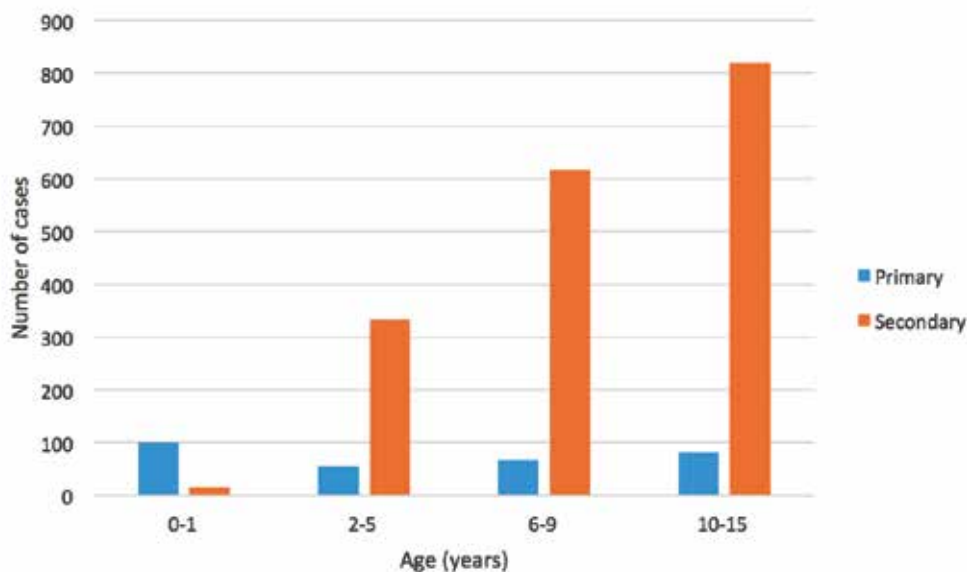


Fig 4—Serological response of dengue patients at King Chulalongkorn Memorial Hospital between 1987 and 2007.

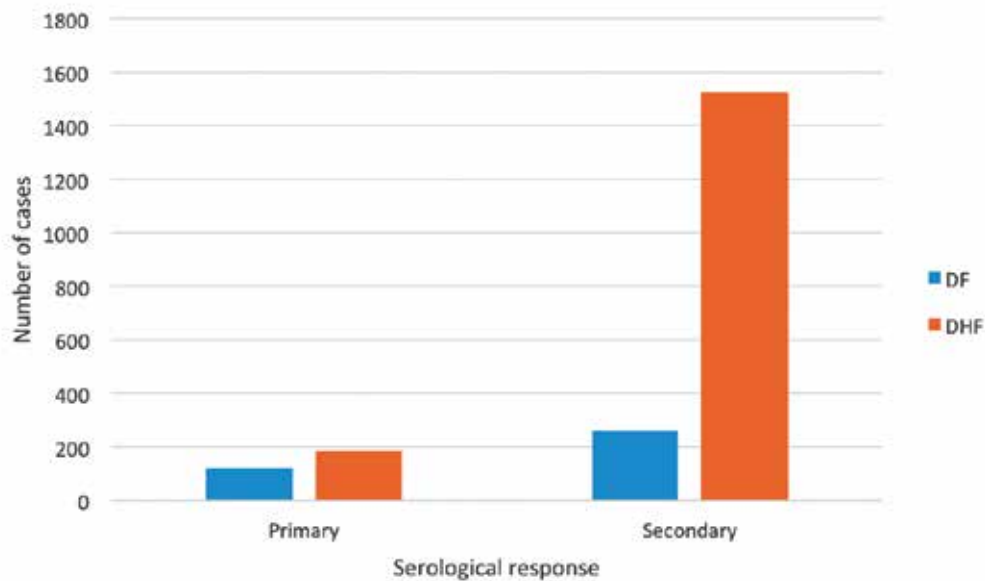


Fig 5—Serological response vs dengue severity in dengue patients in King Chulalongkorn Memorial Hospital between 1987 and 2007.

DISCUSSION

Our study shows a progressive shift in age distribution of dengue patients from early childhood to older children during the past decades which is similar to other studies (Tanayapong, 2013; Nunthanid and Tiawilai, 2015). The rising age of dengue patients has been associated with demographic transition, modern housing and commercial development (Kittigul *et al*, 2007). Dengue patients can be seen all year round with a higher incidence in the rainy season, this usually peaks 2-4 weeks after the arrival of the rains which began anytime between June and September. The rainy season in Thailand usually finishes in October, but can last into November (Tanayapong *et al*, 2013). Several clinical characteristics of dengue disease in the early childhood may be different from the older children. Abdominal pain, one of warning signs for severe dengue (WHO, 2009) was more common in older children who are more likely to be able to report their symptoms better than younger children. Seizures, upper respiratory symptoms and diarrhea were more common in children aged less than 1 year. Many infants with dengue infection have severe organ involvement such as central nervous system which may

result in missed or delayed diagnosis. Exhaustive investigations are usually needed in these cases (Thisyakorn and Thisyakorn, 2015b). A higher mortality rate in infants in this study may reflect a severe organopathy which may have happened in this age group. In addition, 25% of infants in this study had seizures which also are more common due to the febrile convulsions in infants. In dengue endemic areas patients with encephalitis and encephalopathy should be investigated for dengue infection whether or not they have other features of dengue disease (Thisyakorn and Thisyakorn, 1994; Thisyakorn *et al*, 1999; Solomon *et al*, 2000).

A severe form of dengue known as DSS was first recognized in outbreaks of dengue in Southeast Asia in the mid-1950s and was initially thought to be previously unknown manifestation of dengue infection. The hypothesis that the disease is more severe if an infection with one dengue serotype follows infection with another serotype was proposed in the mid-1960s to explain an appearance of DSS (Halstead *et al*, 1967). In this study, all severity of dengue diseases can be seen in all age groups no matter they acquired primary or secondary dengue infection. This confirmed the observation that DSS can occur with primary dengue

infection in all age groups and a second dengue infection is not essential for the development of DSS in person of any age. Most infants in this study acquired primary dengue infection and also resulted in all dengue severity. It is now generally agreed that the syndrome was not new but was only more prevalent than in the past (Rosen, 1989).

Specific antiviral medications are not available for dengue and successful treatment, which is mainly supportive, depends on early recognition of the disease and careful monitoring for shock. Laboratory diagnosis includes virus isolation, serology, and detection of dengue ribonucleic acid. Since dengue poses a heavy economic cost to the health system and society, the potential economic benefits are associated with promising dengue prevention interventions such as dengue vaccine and vector control innovations. (Horstick and Ranzinger, 2015; Thisyakorn and Thisyakorn, 2015c).

In summary dengue is one disease entity with different clinical manifestations, often with unpredictable clinical evolutions and outcomes. Clinical profiles show a difference in some aspects across all age groups. Successful treatment which is mainly symptomatic and supportive depends on early recognition of the disease and careful monitoring for the disease severity. Recognition of clinical characteristics in different age groups are essential in early diagnosis of dengue disease.

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