EPIDEMIOLOGY OF DENGUE AT THAMMASAT UNIVERSITY HOSPITAL DURING 2006-2015

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Abstract. Dengue is the most common mosquito-borne viral disease in humans. Over the past several years, the epidemiological profile of dengue has been changing progressively and is currently characterized by an increase in the number of cases in adults. Between 2006 and 2015, there were 5,633 dengue patients at Thammasat University Hospital (TUH) including 4,132 (73.4%) with dengue fever (DF), 1,501 (26.6%) with dengue hemorrhagic fever (DHF). Of all dengue patients, 3,542 (62.9%) were treated in the outpatient department (OPD), and 2,091 (37.1%) were treated in the inpatient department (IPD). During the years 2006 to 2015, 1,540 cases (27.3%) were children (aged <15 years), and 4,093 cases (72.7%) were adults. The highest numbers of dengue cases were reported in individuals aged 15-19 years (17.5%), followed by 20-24 years (17.1%), and 10-14 years (13.3%). Rates have constantly been high amongst adolescents and young adults (aged 10-24 years). The overall case fatality rate from dengue was 0.1%. The case fatality rate was higher for children (0.19%) than for adults (0.07%). The epidemiology has certainly changed and appears to be shifting from child to adult aged population. However, children still remain at risk for infection and death. This changing epidemiology is important for our public health control programs.

Keywords: age distribution, dengue, dengue hemorrhagic fever, epidemiology

INTRODUCTION

Dengue is the most common mosquito-borne viral disease in the world. The number of dengue cases worldwide reported annually to the World Health Organization (WHO) has increased from 0.4 to 1.3 million in the decade 1996-2005, reaching 2.2 million in 2010 and 3.2 million in 2015 (WHO, 2012; 2016). The incidence of dengue fever (DF)/,dengue hemorrhagic fever (DHF) has continuously increased since the first recognized outbreak in 1958 in Thailand (Halstead *et al*, 1963; Halstead, 1990). By the late 1970s, the disease was widespread among countries in Southeast Asia and DHF had become a leading cause of hospitalization and death among children in Thailand (WHO, 1986).

Four closely related dengue serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) cause the disease, which ranges from asymptomatic infection to undifferentiated fever, DF, and DHF. DHF is characterized by fever, bleeding diathesis, and a tendency to develop a potentially fatal shock syndrome (Thisyakorn and Thisyakorn, 2015). Currently, there are no specific medications to treat a dengue infection. This makes prevention the most crucial weapon in the fight against this disease. The availability of a safe, efficacious, and cost-effective vaccine would significantly alter the paradigm of dengue prevention.

The first dengue vaccine (CYD-TDV) was registered in several countries in 2015. It was registered for use by individuals, 9-45 years-of-age living in endemic areas. Pooled vaccine efficacy amongst all participants aged 9 years or over was 65.6%, and it was 44% in participants aged <9

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Table 1. Epidemiology of dengue at Thammasat University Hospital (2006-2015).

Characteristic	2006 No. (%)	2007 No. (%)	2008 No. (%)	2009 No. (%)	2010 No. (%)	2011 No. (%)	2012 No. (%)	2013 No. (%)	2014 No. (%)	2015 No. (%)	Total No. (%)
Sex	228	263	385	298	291	280	261	332	217	392	2,947
Male	(53.6)	(53.7)	(52.2)	(52.7)	(51.6)	(53.8)	(51.0)	(51.6)	(49.1)	(53.5)	(52.3)
Age, mean, years	26.3	29.1	24.9	24.6	24.4	24.7	22.4	22.5	24.2	24.5	24.8
Age group											
Children	99	107	154	156	162	164	179	215	124	180	1,540
	(23.3)	(21.9)	(20.9)	(27.6)	(28.7)	(31.5)	(34.9)	(33.5)	(28.0)	(24.6)	(27.3)
Adult	326	383	583	410	402	356	333	429	318	553	4,093
	(76.7)	(78.1)	(79.1)	(72.4)	(71.3)	(68.5)	(65.1)	(66.5)	(72.0)	(75.4)	(72.7)
Hospitalization	246	287	411	216	165	143	156	179	56	232	2,091
	(57.9)	(58.6)	(55.8)	(38.2)	(29.3)	(27.5)	(30.5)	(27.8)	(12.7)	(31.7)	(37.1)
Type of infection											
DF	258	297	419	365	384	351	372	511	375	584	4,132
	(60.7)	(60.6)	(56.9)	(64.5)	(68.1)	(67.5)	(72.7)	(79.3)	(84.8)	(79.7)	(73.4)
DHF	167	193	318	201	180	169	140	133	67	149	1,501
	(39.3)	(39.4)	(43.1)	(35.5)	(31.9)	(32.5)	(27.3)	(20.7)	(15.2)	(20.3)	(26.6)

DHF, dengue hemorrhagic fever; DF, dengue fever.

years (Capeding *et al*, 2014; Villar *et al*, 2015). Age and seropositivity were highly correlated in the trials.

Generally, dengue used to predominantly affect children. Evidence-based decision-making on the introduction of vaccines and their use requires not only data on vaccine product characteristics (safety, efficacy, and cost), but also information on effective vaccination, their likely impact on disease burden, and cost effectiveness.

Endemic countries must have a rationale for deciding which segments of the population to protect when national resources or vaccine supplies are scarce. Therefore, an understanding of epidemiological differences in infection rates and severity of disease is important for public health control programs. Most published data are available for dengue hospitalizations, but are lacking for dengue non-hospitalized cases. The aim of this study was to describe the epidemiological pattern of dengue patients, both hospitalizations and non-hospitalizations, in a tertiary care teaching hospital in Thailand from 2006 to 2015.

MATERIALS AND METHODS

A retrospective study was conducted among patients with dengue infection who attended Thammasat University Hospital (TUH), Thailand from January 2006 to December 2015. The diagnosis of dengue patients adhered to the criteria established by the WHO (1997). The data were collected from the hospital database of patients diagnosed with DF, DHF or dengue shock syndrome (DSS).

The study protocol was approved by the Ethics Review Committee of the Faculty of Medicine, Thammasat University.

Data were analysed using descriptive statistics including frequency, percentage, range, mean and standard deviation.

RESULTS

Between 2006 and 2015, there were 5,633 dengue patients at TUH including 4,132 (73.4%) with DF, and 1,501 (26.6%) with DHF; 2,947 (52.3%) were males and 2,686 (47.7%) were females (Table 1). There were 3,542 (62.9%) from the outpatient department (OPD) and 2,091 (37.1%) from inpatient department (IPD) (Fig 1).

The number of dengue cases reported during the years 2006 to 2015 varied from a lowest of 425 in 2006 to a highest of 737 in 2008 (Fig 2). Peaks in dengue cases occurred in the years 2008, 2013, and 2015. Dengue patients were reported throughout the year (Fig 3). The incidence was highest during the rainy season and usually peaked between May and September with the exception of 2015, which had a peak during October to December.

Figs 4 and 5 show dengue prevalence by age groups. During the years 2006 to 2015, 1,540 cases (27.3%) were children (<15 years old) and 4,093 (72.2%) were adults. The highest numbers of dengue cases were reported in individuals aged 15-19 years (17.5%), followed by 20-24 years (17.1%), and 10-14 years (13.3%). Rates have constantly been high amongst 10-24 year olds.

According to the data on the age distribution of DHF, the highest numbers of DHF cases were reported in those aged 20-24 years (17.5%), followed by 25-29 years (15.5%), 15-19 years (15.4%), 30-34 years (9.7%), and 10-14 years (9.6%) with adolescents and young adults representing approximate 70% of reported cases (Fig 6). The hospitalization rate was highest in adults aged 25-29 years (46.6%), followed by those who were 10-14 years (41.7%) and 30-34 years (41.3%) of age.

Fig 7 shows the dengue prevalence in children. Reported cases increased in older children, of which the 13-14 year-old age group was most affected.

The overall case fatality rate from dengue was 0.1% (*n*=6). The case fatality rate was higher for children (0.19%) than for adults (0.07%).

DISCUSSION

In our retrospective study among patients with dengue infection from January 2006 to December 2015, the annual incidence rate of dengue varied

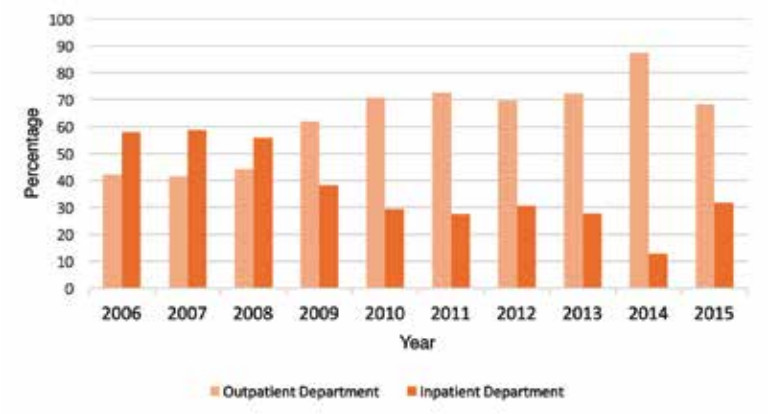
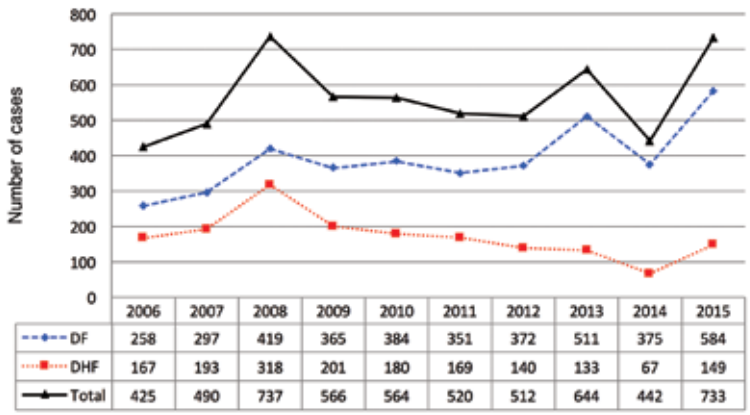


Fig 1–Reported cases of dengue at the outpatient department and the inpatient department, Thammasat University Hospital, 2006-2015.



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
DF	258	297	419	365	384	351	372	511	375	584
DHF	167	193	318	201	180	169	140	133	67	149
Total	425	490	737	566	564	520	512	644	442	733

DHF, dengue hemorrhagic fever; DF, dengue fever.

Fig 2–Reported cases of dengue fever and dengue hemorrhagic fever at Thammasat University Hospital, 2006-2015.

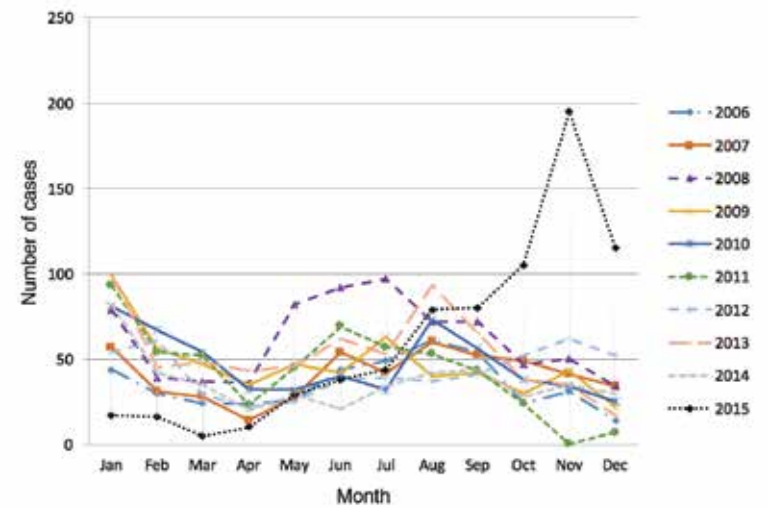


Fig 3–Number of reported cases due to dengue by month at Thammasat University Hospital, 2006-2015.

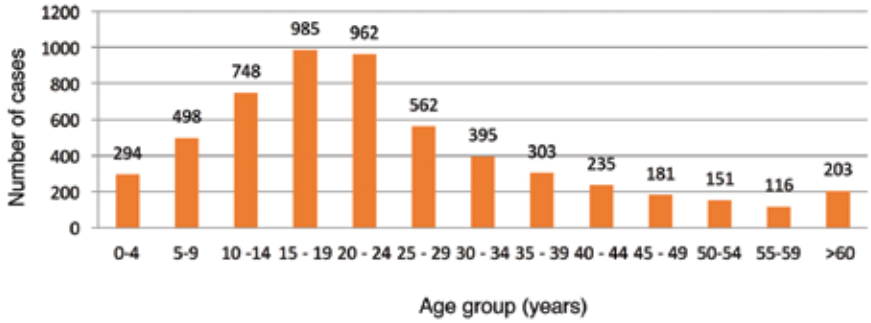


Fig 4–Reported cases of dengue by age group at Thammasat University Hospital during 10 years from 2006-2015.

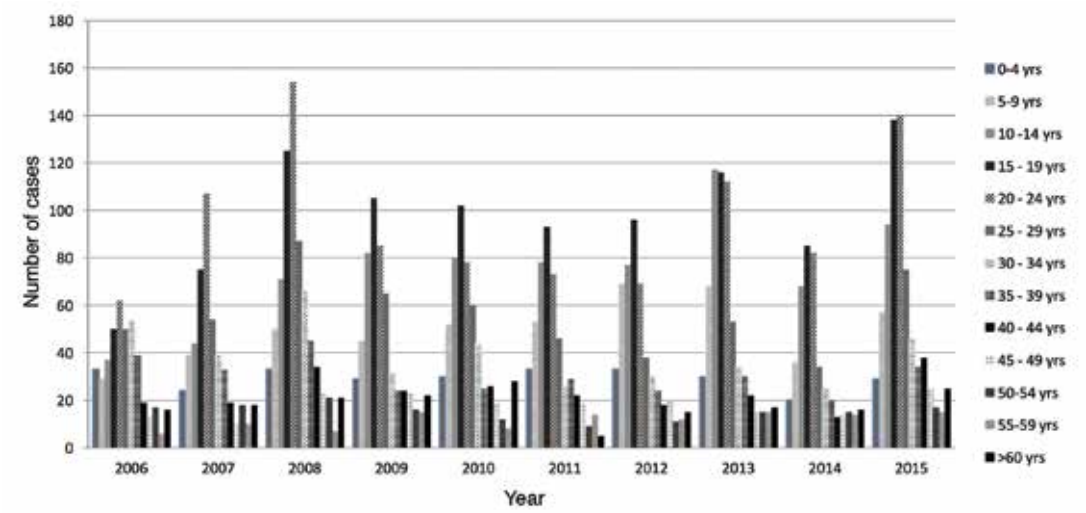
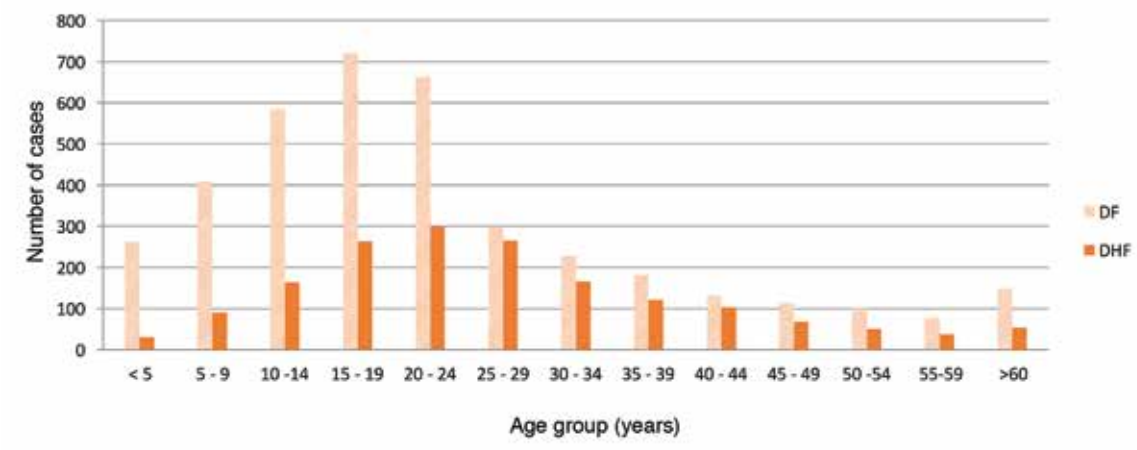
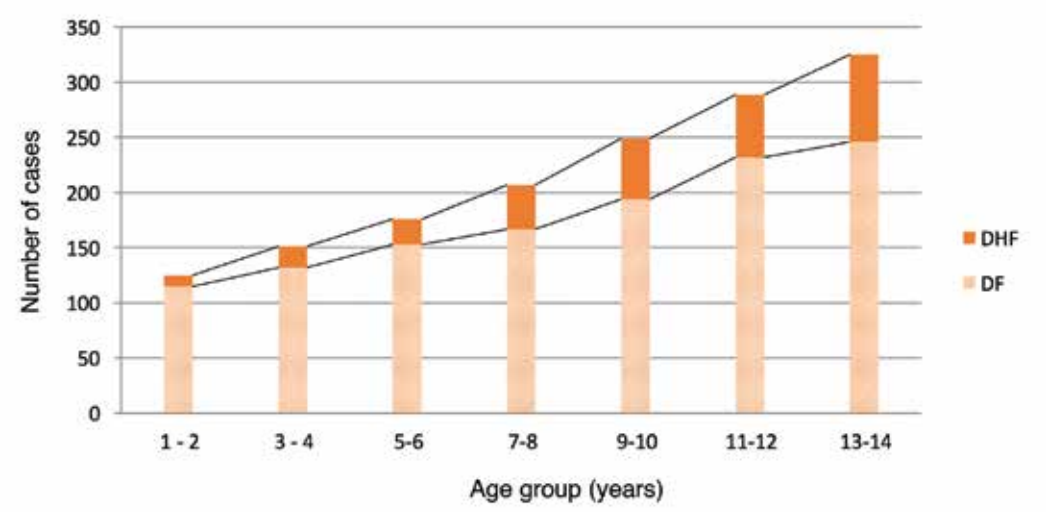


Fig 5–Age distribution of dengue, 2006-2015.



DHF, dengue hemorrhagic fever; DF, dengue fever.

Fig 6–Reported cases of dengue fever and dengue hemorrhagic fever across different age groups during 2006-2015.



DHF, dengue hemorrhagic fever; DF, dengue fever

Fig 7–Number of dengue fever and dengue hemorrhagic fever in children during 2006-2015.

during the 10-year period. The highest numbers of dengue cases were reported in adolescents and young adults (10-24 years old). Historically, dengue was predominantly a pediatric disease, but the number of adult patients has been increasing in the last decade. Several studies in both Latin America and Southeast Asia have reported a higher association of DHF with older ages (Sapir and Schimmer, 2005; Ooi and Gubler, 2008; Cummings *et al*, 2009; Beatty *et al*, 2010; Martin *et al*, 2010; Bravo *et al*, 2014; Karyanti *et al*, 2014; Mohd-Zaki *et al*, 2014).

A literature survey was conducted by Limkittikul *et al* (2014) to shady the epidemiology of dengue in Thailand between 2000 and 2011. This review showed a shift in age group predominance towards older ages, which also continued through the review period. Disease incidence and deaths remained highest in children aged ≤15 years. Other studies in Thailand showed affected adults >15 years of age comprised 30-40% of dengue cases (Patumanond *et al*, 2003; Simmons *et al*, 2010). Many studies have only concentrated on cases that have hospitalizations. One strength of our study was the inclusion of both hospitalized patients and non-hospitalized patients, which indicated that the dengue was predominantly (73%) in the adult age group.

Comparing the hospitalization for dengue in children and adults, we found that the numbers are still highest in the adult age group. Increased mobility of the adult population in our country, better access to health care facilities, improved reporting, and ease of reporting to physicians might be some of the factors of high incidence of dengue among adults. This changing epidemiology is important for public health control programs. We believe that awareness about the shifting age-pattern is not only essential for clinical and public health vigilance, but also for the efficiency of preventive strategies. Education for the public on dengue awareness in the adult age group could improve timely medical interventions. Furthermore, national dengue immunization programs should consider the epidemiological data about the burden of disease.

Dengue infection depends on the seasonal variation of the climate. Standing water from rainfall provides places for the mosquitoes to lay their eggs and develop to the adult stage. Wu *et al* (2009) showed that with every 1°C increase in the monthly average temperature in Taiwan, the total population at risk for dengue fever transmission would increase by 1.95 times. Dengue is endemic in Thailand; Peak transmission rates occur in

the rainy season, between May and September (Limkittikul *et al*, 2014). Our study confirmed a seasonal pattern of dengue with the majority of cases occurring during the rainy season. However, our results showed an outbreak from October-December only in 2015, which was not the rainy season.

Climatic changes resulting in increased temperature and rainfall together with urbanization may therefore be associated with increased dengue incidence and outbreak risk (Khasnis *et al*, 2005). Thailand is a tropical country with a relatively high temperature and humidity all year-round. These conditions are ideal for *Aedes* mosquitoes to have established themselves. The potential for the dengue transmission requires the following four factors: (1) a number of susceptible humans, (2) a number of mosquitoes, (3) virus transmission potential, and (4) a suitable climate (Polwiang, 2015).

There are several limitations to our study. First, our retrospective study design relies on reports dependent on the clinician's documentation. Also, the number of cases may be over-diagnosed because this study did not use serological laboratory-confirmation for diagnosis. Third, specific incidences of DHF were not classified according to severity. Another limitation was the lack of serotyping of the reported dengue cases. Notably, TUH was closed from October 22, 2011 to November 14, 2011 due to severe flooding in the region. On November 15, 2011, the hospital was only operating at partial capacity for a month; for example, some floors were temporarily shut due to flooding, and some OPDs were moved to another location. This would have affected the patient records during this period of time.

Dengue remains a major public health concern in Thailand. The epidemiology in this region has certainly changed and appears to be shifting from children to adult age group. However, children still remain at risk for infection and death. Epidemiological and virological surveillance of dengue in Thailand should be improved so that we have a better knowledge base on how to control it. Most importantly, more research is needed on affected age groups and vaccine use, as well as specific serotype and weather conditions for mosquito breeding.

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