

Introduction

Worldwide, dengue has been an important vector-borne disease transmitted mainly by *Aedes* mosquitoes, particularly *Aedes aegypti*. Four serotypes of dengue virus, including DEN-1, DEN-2, DEN-3 and DEN-4, have been circulating in Thailand over decades.

In Thailand, dengue hemorrhagic fever (DHF) was first reported since 1958^[1], and the disease was mainly occurred in children below 15 years of age with the highest morbidity of 325/100,000 population in 1987. Young school-age children at 5-14 years were at the highest attack rate of dengue fever (DF) and dengue hemorrhagic fever (DHF)^[2]. The clinical characteristics of dengue infection are classified into 3 categories, including DF, DHF and dengue shock syndrome (DSS). From the previous studies, proportions of asymptomatic dengue infection was significant both in children (40%)^[3] and adults (45%)^[4]. The case fatality rate of dengue infection in Thailand was reducing from 0.85% in 1986 to 0.15% in 2005^[5].

A recent study by Kantachuvessiri reported that the numbers of reported dengue cases have increased in Thai adults^[6]. In addition, data from the national

disease surveillance maintained by the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand showed that proportion of dengue cases among adults aged over 15 years has been increasing from 9.2% in 1996 to 47.7% in 2005 (Figure 1).

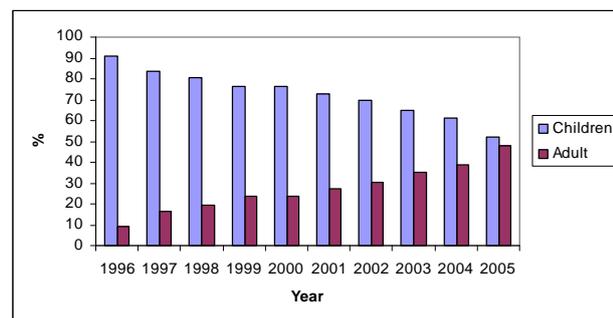


Figure 1 Proportion of dengue cases in children and adult patients reported to the national disease surveillance, Bureau of Epidemiology, Thailand, 1996-2005.

During April-May 2006, two family clusters of dengue illness were admitted in a community hospital of Sukhothai Province in the northern part of Thailand. Dengue infection was confirmed in 3 out of 4 family members and 4 out of 4 from each family cluster lived in two distant villages. Because of high infectivity rate and severity of symptoms, we conducted a field investigation to promptly evaluate the magnitude of disease occurrence, determine risk factors of the outbreaks and implement control measures for preventing further cases in these two villages.

Methods

Case Finding

Cross-sectional serosurveys were carried out in the two affected villages (Village I and II) in order to actively find other dengue cases on 19 and 20 May 2006

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respectively. Villagers were interviewed by a standard questionnaire with assistance from trained village health volunteers. We also searched for cases of dengue-like illness in two local health centers. After obtaining oral consent, single serum samples were collected from all villagers who were residing in the villages.

Case Definition

A case definition was applied from the WHO clinical criteria for dengue infection in 1997 [7]. Results of laboratory tests were classified into 3 categories as follows:

DF was an acute febrile illness for 2-7 days with two or more of the following manifestations: headache, retro-orbital pain, myalgia/arthralgia, rash, hemorrhagic manifestation and leucopenia, and must met the laboratory confirmation by serology.

DHF was a case with two or more clinical criteria of the following manifestations: acute high grade continuous fever for 2-7 days, hepatomegaly, circulatory disturbance of hypotension or narrowed pulse pressure (≤ 20 mmHg) or tachycardia (HR > 120 beat per min) or cold and clammy skin and restlessness, and bleeding manifestations. In addition, the patient developed thrombocytopenia (platelet count $< 100,000$ cells/cu.mm) and evidence of plasma leakage, $> 20\%$ rise in hematocrit for age and sex or $> 20\%$ drop in hematocrit following treatment with fluids as compared to baseline or signs of plasma leakage (pleural effusion, ascites or hypoproteinemia). Finally, the patient must met the laboratory confirmation by serology.

DSS was a case with laboratory confirmed DHF grade III and IV.

Laboratory Testing

The single serum specimens taken from the serosurvey in both villages were sent to the Arbovirus Section at the National Institute of Health (NIH) for dengue-captured ELISA test. The paired serum samples collected from cases in hospital were also sent to the NIH for dengue-captured ELISA testing. Criteria of dengue

infection by ELISA method was applied from the Arbovirus Section in NIH and was defined as the following:

Single serum: If IgM ≥ 40 units, a case was defined as 'acute dengue infection'

and/or IgG ≥ 80 units was defined as 'recent dengue infection'

Paired sera: four-fold rising of dengue IgM and/or IgG

Criteria of primary and secondary dengue infections were defined as the following:

Primary dengue infection:

1. *Single serum:* IgM ≥ 40 units with any value of IgG and IgM:IgG ratio ≥ 1.8 (Duration between onset and date of blood drawn was more than 7 days)

2. *Paired sera:* IgM > 40 units in first serum and second serum IgM < 40 units (Duration of onset and second blood taken was more than 17 days)

Secondary dengue infection:

1. *Single serum:*

1.1 IgM ≥ 40 units with any value of IgG and IgM:IgG ratio < 1.8

(Duration between onset and date of blood drawn was 7-17 days) or

1.2 IgM < 40 units and IgG ≥ 80 units

(Duration between onset and date of blood drawn was less than 17 days)

2. *Paired sera:* IgM < 40 units and IgG ≥ 80 units and two-fold rising of IgG (Duration of onset and second blood taken was 7-17 days)

Cross-sectional Analytic Study

A questionnaire was used to interview people in two villages. It consisted of demographic data, dengue-related clinical illnesses and risk factors, including travel history. Our study recruited all villagers who were residing in the villages at the time of investigation.

Environmental and Entomological Study

Every household in the villages was visited by the village health volunteers and investigation team members. We walked home-to-home for exploring the potential sources of infection both in-home and surrounding areas, and identified mosquito larvae in water-filled containers. Breteau index was calculated to determine the mosquito density and subsequently collected for identification of mosquito species by entomologists at the Office of Disease Prevention and Control Region 9 in Phitsanulok Province.

Statistical Analysis

Univariate analyses were conducted by using Epi Info version 3.3.2 (CDC, Atlanta, USA). Chi-square test was performed to identify differences between proportions of children and adult cases. Multiple logistic regression was used in the multivariate analysis.

Results

Village I and Village II were in rural and mainly agricultural area. Village I had relatively more population than Village II (80 vs 57). Village II was far from the main road for 5 kilometers and was surrounded by agricultural fields. Totally, 107 individuals from the 137 eligible populations (78.1%) in both villages were surveyed, which included 54/80 (67.5%) in Village I and 53/57 (93.0%) in Village II.

Overall, there were 26 dengue infections confirmed by laboratory test. Village I had 19 cases of dengue infection and Village II had 7 cases. The laboratory results were shown in table 1. Mean age of dengue infected persons was 29.1 ± 22.0 years and 20.5 ± 7.8 years in Villages I and II respectively. [Median 20 years (2-74) and 18 years (12-33) in Villages I and II respectively] Overall mean age of dengue infected persons in both villages was 26.8 ± 19.5 years with sex-specific attack rate 23.8% and 26.5% in males and females respectively. The most common clinical characteristic was asymptomatic (46%) and followed by DF (38%), DHF (12%) and DSS (4%). There were 14 symptomatic cases from Village I (10) and Village II (4) (Figure 1).

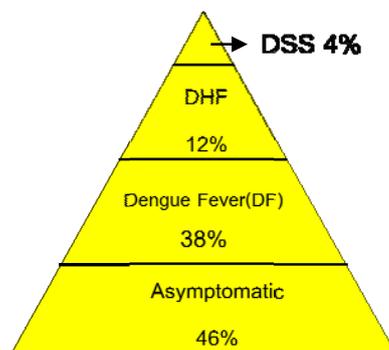


Figure 1 Clinical characteristics of all dengue infection outbreaks in Villages I and II, Kongkraitas District, Sukhothai Province, April-May 2006

All 7 hospitalized cases identified as DF (3), DHF (3) and DSS (1) were confirmed as acute secondary dengue infection. Overall 26 confirmed dengue infections were mostly secondary infection (88.5%), with 84.2% and 100% for Villages I and II respectively.

Age-specific attack rate among children aged below 15 years and adults was not statistically different in both villages (Figure 2).

Risk factors of dengue infection of both villagers were included to be single study. Crude prevalence rate ratio was carried out and shown in table 2, and multivariate analysis was shown in table 3.

Hundreds of mosquito larvae collected from patients' houses were subsequently identified as *Aedes aegypti* while mosquito larvae collected from surface water near the patients' houses were identified as *Culex* mosquito and *Aedes aegypti*.

Discussions

Progression of age-shift among dengue cases (only for symptomatic) in Thailand was noted from 1960 to 1980^[8]. Moreover, a recent study in Thailand conducted at Chonburi Regional Hospital, which was identified as epidemic area during 2001, revealed that the most frequent age group was 10-14 years old^[9]. The data from national notifiable disease report of dengue infection from 1996 to 2005 showed that proportion among children and adult cases were nearly 50% (1.09:1) and median age was 14 years old

(range 10-23 years old) in 2005. In some countries like Singapore, proportion of dengue case changed since 1981^[10] and Cuba in 2001-2002 showed that maximum incidence was among 25-34 years old group^[11]. The hospital data of dengue cases was not reliable due to bias of diagnostic for dengue because pediatricians were almost always concern of dengue infection than internists and thus, lab confirmation among children was higher^[9]. This study was conducted in real situation when dengue cluster was detected in 2-3 cases and serosurvey revealed high number of cases in adults with statistically insignificance.

Even though the attack rates in both villages (19% vs 33%) were less than that of previous reports (40-50%)^[12], it might be due to lack of second blood testing during serosurvey and some people might already have immunity to prevent the infection. However, this investigation results demonstrated high attack rate among both children and adult groups accompanying the passive surveillance data for the nationwide. We believed that all age groups were susceptible to dengue infection as chance of getting infected might not directly related to

age, but it might associate with daily activities and environment that prone to have infection as appeared in this study, including living in area with many mosquito larvae, visiting dengue case to their home, having dengue patient in the house and visiting to the grocery store.

As the Breteau indices were high for both villages, it indicated that villagers might be infected with dengue virus previously and serologically confirmed cases proved high percentage of secondary dengue infection (88.5%).

According to the results, we acted directly on eliminating mosquito larvae and its habitat by walking door-to-door in both villages for mosquito elimination campaign. We also inspected weekly for 3 weeks. The successful outbreak control was mainly assisted by community leaders and all villagers in the villages.

Acknowledgement

We would like to thank all the local staff at Kongkrailas Community Hospital and village health volunteers who assisted in the investigation and health education campaign.

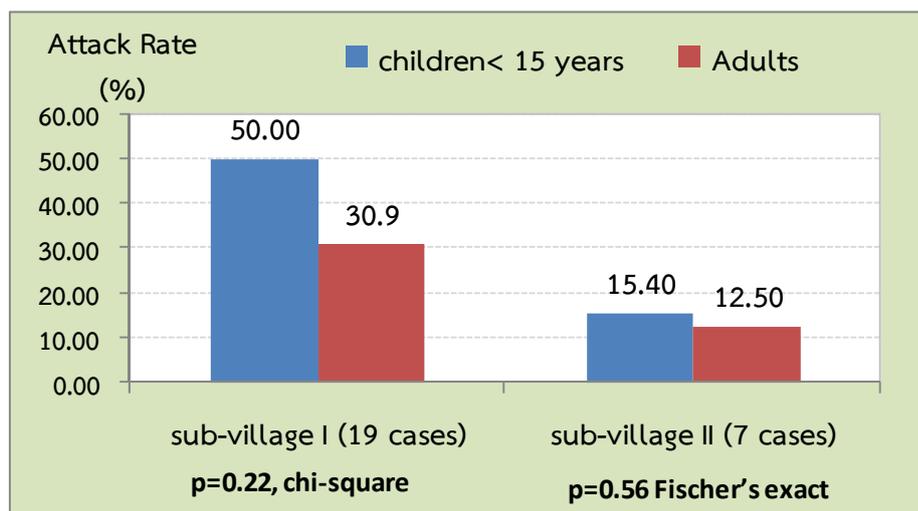


Figure 2 Attack rate of dengue infection among children <15 years and adults in Villages I and II, Kongkrailas District, Sukhothai Province, Thailand, April-May 2006

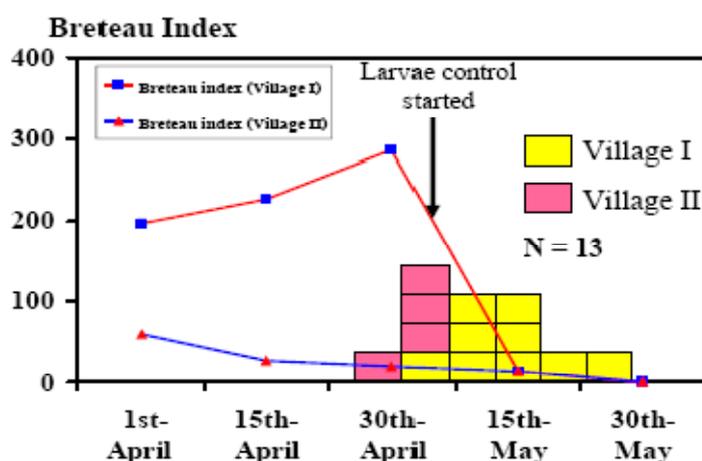


Figure 3 Epidemic curve of dengue cases by date of onset and Breteau index in Villages I and II, Kongkraitas District, Sukhothai Province, Thailand, April-May 2006

Table 1 Serological testing by dengue-captured ELISA among residents in Villages I and II, Kongkraitas District, Sukhothai Province, Thailand, 2006

	Village I	Village II
Number of population	80	57
Number of resident tested	54	53
Hospitalization*	4	3
Number of ELISA confirmation	19	7
1.1 Acute infection	11	2
1.2 Recent infection	8	5
2.1. Primary infection	3	0
2.2. Secondary infection	16	7

* Only hospitalized patients were confirmed by paired sera for antibody-captured ELISA

Table 2 Univariate analysis on risk factors of dengue infection outbreak in Villages I and II, Kongkraitas District, Sukhothai Province, Thailand, April-May 2006

Factor	Ill (No.)	Not-ill (No.)	PR	95% CI	p-value
Sex: male	6	31	0.6	0.2 – 1.3	0.15
Age: children <15 years	8	17	1.5	0.7 – 2.9	0.30
Having at least one child in household	19	54	1.4	0.6 – 3.3	0.38
History of visit to dengue case	16	26	2.5	1.2 – 4.9	< 0.01
Having a household member with dengue infection	11	3	4.8	2.8 – 8.3	< 0.01
Frequent visits to the grocery store	17	28	2.6	1.3 – 5.3	< 0.01
Living in Village I (high BI)	19	35	2.7	1.2 – 5.8	< 0.01
Living at home during daytime	20	49	1.8	0.8 – 4.1	0.13
Living at home >12 hours	18	50	1.3	0.6 – 2.7	0.50
Crowded household (>4 persons)	7	26	0.9	0.4 – 1.8	0.70

Table 3 Multivariate analysis on risk factors of dengue infection outbreak in Villages I and II, Kongkraitas District, Sukhothai Province, Thailand, April-May 2006

Factor	Crude PR	95% CI	Adj. OR	95% CI	p-value
Age: children <15 years	1.5	0.7 – 2.9	1.2	0.3 – 4.7	0.82
History of visit to dengue case	2.5	1.2 – 4.9	1.3	0.4 – 4.7	0.60
Having a household member with dengue infection	4.8	2.8 – 8.3	119.9	9.1 – 1567.4	< 0.001
Frequent visits to the grocery store	2.6	1.3 – 5.3	3.4	0.9 – 12.4	0.06
Living at home during daytime	1.8	0.8 – 4.1	0.9	0.2 – 3.4	0.91
Living in Village I (high BI)	2.7	1.2 – 5.8	15.0	1.7 – 128.6	< 0.001

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Changing Epidemiology of Dengue Infection in Thailand: Evidence from an Outbreak Investigation in Rural Villages of Sukhothai Province, Thailand, 2006.

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Abstract:

Background: Dengue has been an endemic disease in Thailand for decades and it mainly affects children under 15 years. During April-May 2006, two family clusters (3/4 and 4/4) of dengue disease were detected in two rural villages of Sukhothai Province, the northern Thailand. We conducted investigations to identify risk factors of the outbreak and implement control measures.

Methods: Active case finding was conducted in the two affected villages. Case definition was applied from the WHO clinical criteria for dengue diagnosis and laboratory confirmation by capture ELISA IgM and IgG in single or paired serum specimens. A cross-sectional dengue seroprevalence survey was conducted. Blood specimens and information were collected from 54 and 53 villagers of Village I and II respectively. Environmental and entomological investigations were carried out. Multivariate analysis was performed.

Results: All cases of DF (3), DHF (3) and DSS (1) were laboratory confirmed for acute secondary dengue infection. Dengue infection rates were 35.2% in Village I and 13.2% in Village II. Number of dengue infected cases (symptomatic/asymptomatic) were 19 (5/14) and 7 (4/3), and mean age was 29.1 ± 22.0 years and 20.5 ± 7.8 years in Village I and II respectively. Age-specific attack rates among children <15 years and adults were 30.9% and 50.0% in Village I, and 15.4% and 12.5% in Village II. Risk factors for acquiring dengue infection included visiting dengue patient (PR 2.5; 95% CI 1.2-4.9), having a household member with dengue infection (PR 4.8; 95% CI 2.8-8.3), frequent visits to common places in the village such as grocery store (PR 2.6; 95% CI 1.3-5.3) and living in Village I with high Breteau Index (BI) (PR 2.7; 95% CI 1.2-5.8). Multiple logistic regression showed associations between dengue infection and having a household member with dengue infection (Adjusted OR 119.9; 95% CI 9.1-1567.4), frequent visits to common places (Adjusted OR 3.4; 95% CI 0.9-12.4) and living in Village I with high BI (Adjusted OR 15.0; 95% CI 1.7-128.6). High BI was repeatedly observed in both villages before the outbreak: 196.7, 226.7 and 273.3 in Village I, and 60.0, 26.7 and 20.0 in Village II. Mosquito larvae collected from patients' houses were identified as *Aedes aegypti*.

Conclusion: This dengue outbreak investigation revealed comparatively high infection rates in children and adults. Having a household member with dengue infection was a strong risk factor. Educational message should shift to prevent dengue disease for all ages that are equally at risk of dengue infection. Other control measures including eradication of mosquito larvae in households, avoiding mosquito bite, surveillance of mosquito larvae indices by village health volunteers, and community mobilization through the village leaders were promptly implemented to curtail the outbreak.

Key words: dengue outbreak, changing epidemiology, risk factors, Thailand