CHIKUNGUNYA IN THAILAND: A RE-EMERGING DISEASE?

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Abstract. The first reported case of chikungunya virus diagnosed by serology in Thailand was in 1960 and the last one was in 1991. The disease surveillance system does not specifically include chikungunya cases and the signs and symptoms are similar to these of dengue fever/dengue hemorrhagic fever (DF/DHF), rubella, and fever of unknown origin (FUO); thus cases might often be reported under those diagnoses. During the rainy season of 1995 (Jun-Aug), there were at least 2 reported chikungunya outbreaks which might indicate that it is a re-emerging disease in Thailand. However, there is still limited information and knowledge on some aspects of this disease such as clinical manifestations, subclinical cases, duration of illness, complications, transmission, immunity, and reservoirs. Thus, the objectives of this paper are to describe the epidemiology of chikungunya infection based on outbreak investigations carried out in Khon Kaen (July 1991), Nakorn Si Thammarat (July 1995), and Nong Khai Provinces (August 1995). All three outbreaks occured during the rainy season. The three most common clinical manifestrations were fever with severe althralgia with maculopapular rash. Both sexes and all age groups were affected. Serological results were positive for IgM, with four-fold rises in paired sera, and viral isolation in Nakorn Si Thammarat and Nong Khai. Only in Nong Khai was hemagglutinin inhibition conducted and the results were positive. No deaths were reported. The outbreaks occured in rural villages and all three larval indices (BI, HI, CI) were very high. The possible vectors in these outbreaks were *Aedes aegypti* and *Aedes albopictus*. In the Nong Khai outbreak, blood specimens were taken at the 3-5th day after onset and therefore the proportion of positive results was low. IgM antibody of follow-up cases declined within 3 months, villagers from all three areas with outbreaks mentioned that they had no previous experience of this disease. This suggests that chikungunya infection is a re-emerging disease.

INTRODUCTION

Arthropod-borne viral disease or arboviral can produce several clinical symptoms. There are four major clinical syndromes; an acute central nervous system disease; acute benign fever of short duration; hemorrhagic fever; and polyarthritis and rash. However, patients may present with wide range of sign and symptoms and severity (Adesina and Odelola, 1991; Wilson *et al*, 1991).

In the United States, Powassan encephalitis, St Louis encephalitis, Western and Eastern equine encephalomyelitis, and California serogroup encephalitis are the major types among this group (CDC, 1994). Flaviviruses Bunyamwera, Sandfly fever, and Alphaviruses are the major causes in Africa. The Ebola outbreak is a recent example (Adesina and Odelola, 1991; Beneson, 1990; CDC, 1995 a,b; Watts *et al*, 1994). In the past two years, Barmah Forest disease (alphavirus) played an important role in several epidemics in New South Wales, Australia. Other similar viral diseases have been reported from Australia and include Ross River, Edge Hill, and Stratford (Mackenzie *et al*, 1994; WHO, 1995). In Asia, there have been reports of chikungunya infection from Myanmar and India (Padbidri and Gnaneswar, 1979; Thein *et al*, 1992). The first reported chikungunya virus strain detected in human sera in Thailand was in 1960. During 1974-1976, Gunakasem *et al* (1981) conducted serological surveillance of dengue hemorrhagic fever cases in Thailand and found that chikungunya infection was not significant cause of that clinical syndrome.

The last reported outbreak in Thailand, which resulted in 216 cases, was in 1991 (Kittisriworapod *et al*, 1991). This does not preclude other outbreaks because chikungunya is not specifically reported in the disease surveillance system. In addition, signs and symptoms of this disease are similar to dengue fever/dengue hemorrhagic fever (DF/DHF) and ru-

bella, and probably has been reported under those diagnoses. During the rainy season (June-August) of 1995 there were at least two reported outbreaks which might be indicate that it is a re-emerging disease or they might be due to changing clinical manifestrations with more severe presentation. In Thailand, there remains a lack of information and knowledge on some aspects of this disease such as: clinical manifestrations, subclinical cases, duration of illness, complications, transmission, immunity, and reservoirs. The objectives of this paper are to describe the epidemiology of chikungunya infection using outbreaks investigations in Khon Kaen (July 1991), Nakhon Si Thammarat (July 1995), and Nong Khai Provinces (August 1995).

MATERIALS AND METHODS

This is a descriptive epidemiological study based on three outbreaks investigations (Leanpumkarnkit *et al*, 1955; Yucharean *et al*, 1995; Kittisiworapod *et al*, 1991).

All three reports were reveiwed. Investigators were also interveiwed for more information. The methods that were conducted in those 3 outbreak investigations were (1) review of routine surveillance reports, (2) review of patient cards/medical records; (3) interview hospital staff and health workers; (4) environmental and larval surveys; (5) serological tests for IgM, IgG.

RESULTS

Outbreak recognization

In Nong Khai there were several cases of fever with rash and arthralgia who attended health centers during July 1995, however, the outbreak was not recognised until early August. The physician reported an abnormal increase in patients with fever and rash which were different from DF/DHF seen during the rainy season. Similar to Nong Khai, several cases of patients attended health centers from May 1995 and the outbreak was detected later in July in Nakhon Si Thammarat. In mid July 1991, physicians in Khon Kaen reported an outbreak of fever with rash and arthralgia, however, it was not recognised as an outbreak until early September.

Study design

Epidemiological teams from the Division of Epidemiology, Ministry of Public Health, accompanied by provincial health workers, investigated all three outbreaks. While chikungunya is not a notifiable disease, it does have similar symptoms to fever of unknown origin, DF/DHF, and rubella which are reported. Thus, data for these diseases were reviewed as indirect indicators and no increasing trend for those conditions was found in all three outbreaks. Because there were more suspected cases in villages, community surveys were conducted and active case finding was performed. People who had had or currently had the symptoms of chikungunya infection were interviewed by epidemiologists and some of them had blood taken for viral isolation and serology tests, for IgG and IgM to dengue, Japanese encephalitis, rubella, and chikungunya of the Nong Khai and Nakhon Si Thammarat outbreaks. Only IgG was tested in Khon Kaen because no other serology test was available at that time. Environmental and larva surveys were performed in selected villages.

Descriptive epidemiological results

Seka (Nong Khai), Tayang (Nakhon Si Thammarat), and Wang Hin Lart (Khon Kaen) subdistricts are rural areas with many trees around the houses. The space between houses was 10 and 20 meters. There were 94, 576, and 331 cases in Seka, Tayang, and Wang Hin Lart subdistricts, respectively. A small number of cases were detected in Seka subdistrict because the main objective of this outbreak investigation was to determine the cause of an outbreak as soon as possible and to quickly assess the magnitude of the problem for immediate intervention. Both genders and all age groups were affected. Most cases had fever (92-100%) and severe althralgia (80-98%). However, the proportion with maculopapular rash, which presented all over the body and was irritating, was found to be different in each outbreak. The highest proportion was in Nong Khai (72%), the second in Khon Kaen (50%) but only 21% in Nakhon Si Thammarat had a rash. Other symptoms found in cases from the three outbreaks were headache (56%), joint swelling (29%), vomiting (28%), abdominal pain (13%), and lymp node enlargement (15-30%) (Fig 1). Large joints such as wrists, elbows, knees, ankles, and also interphalangeal joints were affected bilater-

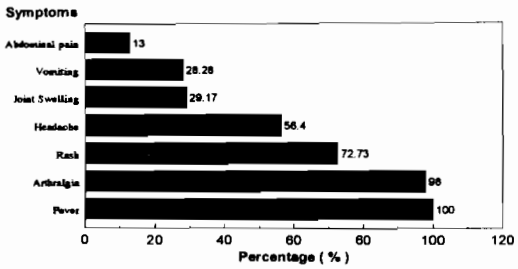

Fig 1–Signs and symptoms of cases, Seka District, Nong Khai: June 1 to August 10, 1995.

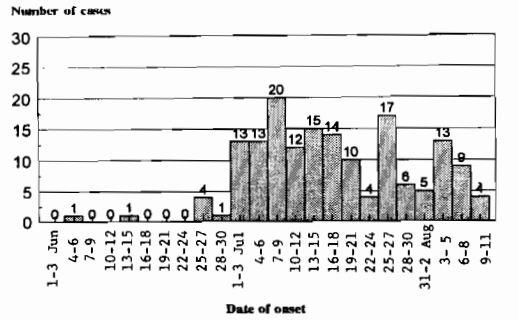

Fig 2–Number of chikungunya cases by date of onset, Village 2, Seka, Nong Khai: June 1 to August 10, 1995.

ally. No death was reported in any outbreak,.

The epidemic curves looked like a propagated sources and the number increased gradually and the majority of cases were in August in all three outbreaks (Fig 2).

There were very high values for 3 indices in the larva surveys. The Breteau indices were above 200 (215-435) and house indices were above 40 (41-93.4) (Tables 1-3). *Aedes aegypti* and *Ae. albopictus* were identified in all outbreaks.

Serological data

Forty-six of 55 cases (84%) in Nong Khai and 31 of 46 cases (67%) in Nakhon Si Thammarat were IgM positive for chikungunya virus. Among the IgM negative cases (16), 9 (56%) were positive for viral isolation in Nong Khai. In Nakhon Si Thammarat, only 13 of 45 blood specimens for viral isolation could be interpreted as some samples were spoilt and none were positive. However, 17 of 19 cases from this province were positive in paired sera. In Khon Kaen, 5 of 13 (39%) among cases had positive paired sera with none among non-cases (0/19) in one village and there were 55% among cases (16/29) with positive paired sera with 12% among non-cases (5/40) in a second village.

Special surveillance

According to active case finding and ongoing chikungunya surveillance in Nong Khai Province, the number of cases declined gradually within 3 months. There were 1,716 cases of fever with rash or arthralgia (without laboratory confirmation) reported from 5 districts in August. Seventy-eight percent (1,333) were reported from Seka District (583 males, 750 females). Among this group, 76% were aged between 10-64 years (range: < 1 year to > 65 years). In September there were only 81 cases reported from 2 districts of which 77 cases (95%) were from Seka District (30 males, 47 females). Among this group, 79% were aged between 10-64

Table 1

Larval survey indices by administrative area, Seka District, Nong Khai Province.

Index	Designated sanitary health district[d] (village 1)	Non-designated sanitary health district (village 2)
Breteau[a]	320	240
Container[b]	43.1	29.6
House[c]	93.3	86.6

[a] Breteau index = number of container(s) with at least one larva in 100 surveyed houses.
[b] Container index = number of container(s) with at least one larva × 100 surveyed containers.
[c] House index = number of house(s) with at least one larva × 100 surveyed houses.
[d] Government provides basic values and sanitation services in these areas.

Table 2

Larva survey indices, Thung Yai District, Nakhon Si Thammarat Province.

Index	Village 5	Village 6
Breteau	215	293.3
Container	58.9	47.8
House	85	93

Table 3

Larva survey indices, Chum Phae District, Khon Kaen Province.

Index	Village A	Village B
Breteau	86.2	435
Container	10.6	57.6
House	41.4	93.4

years (Range: < 1 year to > 65 years). In October only 3 cases were reported from Seka District.

DISCUSSION

At the beginning of all three outbreaks, it was difficult to diagnose which disease was the cause as they occurred in endemic areas for DF/DHF and the maculopapular rash was similar to that seen in other exanthem diseases. In addition, Thai people in rural areas often do not seek medical care at government health centers. They often buy medicines from drug or grocery stores. The outbreaks were recognised not from the disease surveillance system but by physicians and other health workers. However, the data of the disease surveillance system were used to identify what, where, and when the investigation should take place.

Halstead *et al* (1969) noted that children admited to the Children's Hospital in Bangkok with chikungunya had sought medical care within 24-48 hours after onset of symptoms. Initially, they were diagnosed as pyrexia of unknown origin and usually presented with vomiting, abdominal pain, anorexia, pharyngial redness, rhinitis, facial flush, and high fever (Halstead *et al*, 1969). These symptoms are slightly different from those found in the three outbreaks described in this paper, probably because it was a hospital-based study and only children were included, however, changes in clinical presentation cannot be ruled out. Carey *et al* (1969) investigated chikungunya outbreak in South India and found that nearly a third of 39 cases with confirmed chikungunya infection in children were associated with convulsions. Among adults, arthralgia was the most prominent clinical feature. The pain mainly affected the small joints of hands, wrists and feet, and also knees. Patients usually had and developed a maculopapular, irritating rash toward the end of the febrile phase. Patients, also frequently developed enlarged and tender inguinal lymph nodes as was also seen in the outbreak in Nong Khai Province. Cases mentioned severe arthralgia which forced them to remain in bed for many days similar to that reported elsewhere (Adesina *et al*, 1991; Brington *et al*, 1983; Watts *et al*, 1994; Wilson *et al*, 1991; Tesh, 1982; Thein *et al*, 1992). Some had persistent joint pain for several months, similar to other studies (Adesina *et al*, 1991; Brington *et al*, 1983; Halstead *et al*, 1969; Tesh, 1982).

From the community survey, it was found that the houses in the villages were located close together and mosquitos could fly from house to house. There were many containers with water both in and outside the houses. All three larval indices were very high. These indices were principally designed for yellow fever. For the suggestive diag-nosis of which Breteau Index should be less than 50 and the House Index less than 5 which indicate that epidemics might occur if nothing was done to prevent them. However, there is no information on how high they need to be to cause epidemics of chikungunya infection. The possible vector was *Ae. aegypti* and *Ae. albopictus* as reported from other studies (Adesina *et al*, 1991; Brington *et al*, 1983; MacKenzie *et al*, 1994; McGill, 1995; Padbidri and Gnaneswar, 1979). Viral isolation from mosquito was not conducted in any of the three outbreaks.

Carey *et al* (1964) found that chikungunya virus was not recognised as being active in South India before the 1964 epidemic, but subsequent study of pre-epidemic survey sera suggest that the virus was present in the area during the 1930's. Serological studies in Thailand, which was conducted by Gunakasem *et al* (1981) in all provinces showed that chikungunya was not a significant cause of illness

either clinically or laboratory study in the surveillance program and Johnson *et al* (1976, in Prachinburi Province) showed that the prevalence of antibody was age related with a 50% prevalence at about age 45. Since then, there has been no significant in laboratory surveillance (personal communication with A Nisalak). In 1995, there were 3 reported chikungunya outbreaks in 3 provinces. In the Nong Khai outbreak, IgM antibody of follow-up cases declined within 3 months. Viral isolation from blood specimen is appropriate during the first 3 days after onset of symptoms as mentioned in other studies (Carey *et al*, 1969; Halstead *et al*, 1969). But in the Nong Khai outbreak blood specimen were taken at the 3-5th day of onset and consequently the proportion of positive results was low. However, among the IgM negative group, more than half had a positive viral isolation. Villagers from all three outbreaks mentioned that they had no experience of this disease before. This might be further evidence to suggest that chikungunya infection is emerging or re-emerging disease in Thailand. No pre-epidemic serological study was conducted in any of the areas.

In Nong Khai there were many unreported cases which stayed at home in all three outbreaks. Before laboratory results were known, the investigating team had modified the content of DF/DHF information designed for educating people and included the term "fever with arthralgia and rash" for the campaign. Since *Aedes* species are also the vector of DF/DHF and there were high densities in these villages, the investigating team recommended that the health staff take steps to eliminate the breeding places of the vector mosquito with fogged insecticide to control the transmission.

In Africa, baboons are the animal reservoir but in Thailand there has been no investigation of what might be the local animal reservoir. The proportion of subclinical cases is not clear and the relationship between DF and chikungunya is also not established even though dual infection by these viruses has been reported. Finally, the immunology of this disease is not well documented and wether it can prevent reinfection or not and how long immunity lasts. Therefore, further studies are needed to solve these problems, including whether chikungunya is re-emerging in Thailand or not.

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