

Original article

Epidemic of New Chikungunya Viral Genotype and Clinical Manifestations in Thailand, 2008-2009

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Abstract

Introduction This was the first Chikungunya epidemic of the Central-east African genotype in Thailand from 2008 to 2009.

Objective To describe the clinical manifestations and self-care of patients.

Methods Health officers surveyed the affected districts from February to April 2009. There were 421 patients in the two southernmost provinces of Thailand where the epidemic started. Health offices and patients had face-to-face interviews.

Results The majority of patients were women (53.2%); with a median age of 36.0 years (range 12 to 78 years) 69.2% of them had an agricultural occupation. The median duration of illness was 8 days. The three most common complaints were mainly myalgia in 89.3% of patients, joint swelling in 80.7%, and arthralgia in 62.3%. The clinical manifestations included myalgia (96.9%), fever (96.2%), joint swelling (96.0%), headache (92.9%), rash (64.8%), and arthralgia (63.9%). The median days of illness before seeking health care was 2 days (range, 0 to 60). The frequency of seeking health care ranged from 1 to at least 5 times during the illness.

Conclusions Our findings provide useful information for surveillance systems and control programs. In primary health care units, where a laboratory is not available, it may be useful to include myalgia in the case definition. Further studies of complications, immunology, and control measures are needed. **Chiang Mai Medical Journal 2011;50(1):1-11.**

Keywords: Chikungunya, Thailand, clinical manifestation, arthralgia, myalgia, epidemic, Central-east African genotype

The first reported outbreak of Chikungunya occurred in Tanzania between 1952 and 1953.^(1,2) The word Chikungunya means “that which contorts or bends up.” It comes from Kimakonde, the vernacular in Tanzania and Mozambique. It characterizes the contorted posture of the infected individuals, who suffer severe arthralgia with limited capacity for daily life activities.^(1,2) Chikungunya infection is caused by the Chikungunya virus (CHIKV). It is an alphavirus belonging to the *Togaviridae* family.⁽³⁻⁴⁾ Vectors are *Aedes aegypti* and *Aedes albopictus* mosquitoes. The incubation period ranges from 1-12 days, with the disease usually lasting about 2-4 days.⁽⁵⁻⁷⁾

The clinical manifestations include high fever, arthralgia, arthritis, myalgia, maculopapular rash, itching, headache, conjunctiva injection, nausea, vomiting, and petechiae. A characteristic symptom is severe arthralgia, which usually involves more than one joint.^(3,4,7,8) This symptom can sometimes last as long as a year.⁽⁹⁻¹¹⁾ Deaths or neurological complications have occurred in India, the French Réunion Islands, and Cambodia.^(12,13) Severe bullous skin lesions were reported in infants in La Réunion Island.⁽¹⁴⁾

CHIKV is a silent worldwide health threat, which should be cause for great concern. There have been several outbreaks and epidemics in many countries over several continents, including eastern Africa, the western Indian Ocean islands, the eastern Indian Ocean islands, Italy, France, India, Singapore, Indonesia, Malaysia, and Thailand.^(6,15-18) An adaptive mutation of CHIKV, *Aedes albopictus*, can be transmitted effectively via mosquitoes, and is therefore a significant consideration in all human activities, including national and international transportation.^(4,15) Recently, reports have emerged of

CHIKV outbreaks in the Indian Ocean Islands, Asia, Europe, USA, and Australia.^(16,19-23) An important factor in the spread of the virus is population migration.^(16,19,20,22,23) The isolated CHIKV outbreak in India in December 2005 was a Central-east African strain that was closely related to the strain from the Réunion Islands.^(22,24) These CHIKV outbreaks spread rapidly and were followed by long, silent inter-epidemic periods. Some reasons for these widespread epidemics were the intensity of human interaction, insufficient regional control strategies, and lack of immunity against CHIKV in the local people.⁽⁴⁾

The first reported CHIKV infection case in Thailand was in 1958.⁽²⁵⁾ There have been at least 6 documented CHIKV outbreaks in the past 20 years in the northeast and south of the country. The outbreaks occurred in 1988 (1), 1991 (2), and 1993 (3).^(10,11,18) The latest CHIKV epidemic started around August 2008 in Narathiwat province, the southernmost province of Thailand.^(26,27) The investigation of the outbreak was conducted using a case definition based on previous outbreaks in Thailand.⁽¹⁸⁾ The virus had spread to over half of the country (58 out of 76 provinces) by December 2009. There were at least 49,069 cases (77.41 per 100,000 of population) with no deaths.⁽²⁹⁾ The CHIKV strain was reported later as the Central-east Africa genotype.

This is the first time that the CHIKV genotype differed from previous epidemics, which were caused by the Asian genotype.⁽³⁰⁾ Even Thai physicians and medical schools had no experience with the clinical manifestations of this epidemic strain. Misdiagnosis was one of the important factors that contributed to the rapid spread of the epidemic. Due to the nature of the disease, the case defini-

tion and way that infected people took care of themselves were important factors for surveillance systems and prevention and control programs. Unfortunately, as the outbreak spread rapidly, we had to conduct the study amidst terrorism and political unrest in the deep south of Thailand. The difficulty was how to use the existing system to obtain valid information urgently for government control measures. Therefore, this study was conducted in away to describe the clinical manifestations and self-care of patients in the provinces where the Chikungunya epidemic started.

METHODS

The chosen areas were 4 affected districts in 2 provinces where the epidemic started in August 2008. The health officers surveyed the affected districts from February to April 2009. The patients diagnosed as having Chikungunya infection during the early stage of the epidemic were selected from the Primary Health Care Units (PCU), Narathiwat and Songkla provinces. Health personnel involved in epidemic control were trained for interviewing. They visited infected patients in the villages and interviewed them about their illnesses. They asked them about their family and friends, who had similar signs and symptoms, and visited these suspected Chikungunya cases for further interviewing.

The clinical diagnostic criterion was villagers in affected areas who had developed any symptoms or signs during the epidemic period. The symptoms or signs included high fever, arthralgia, joint swelling, myalgia, maculopapular rash, itching, headache, conjunctiva injection, nausea, vomiting, and

petechiae.

Four hundred and twenty one patients participated in this study. The questionnaire included demographic information, chief complaints, clinical manifestations, severity, and self-care.

RESULTS

The majority of patients were women (53.2%); with a median age of 36.0 years (range 12 to 78 years). They had had a primary school education (45.6%) and 62.9% of them had an agricultural occupation (almost all of them worked on rubber plantations). They resided in Ye-ngo (31.4%), Saba-yaoy (26.6%), Nathawe (23.3%), and Sadoa (18.8%) districts of Songkla and Narathiwat provinces.

1. Chief complaints

Among 421 patients, 309 (73.4%) completed data of severe symptoms that caused them to seek health care from health centers, hospitals, clinics, drug stores, or folk medicine. The three most common complaints were mainly myalgia 89.3%, joint swelling 80.7%, and arthralgia 62.3% (Fig. 1).

2. Clinical manifestations

The median duration of illness was 8 days (range, 1 day to 131 days). Patients were ill for usually 2 days (range 0-60) before seeking care. Signs and symptoms included myalgia (96.9%), fever (96.2%), joint swelling (96.0%), headache (92.9%), rash (64.8%), and arthralgia (63.9%).

The patients rated their severity as none, mild, moderate, severe, and very severe. Of the 408 patients who had completed myalgia data, 71.8% had severe to very severe pain

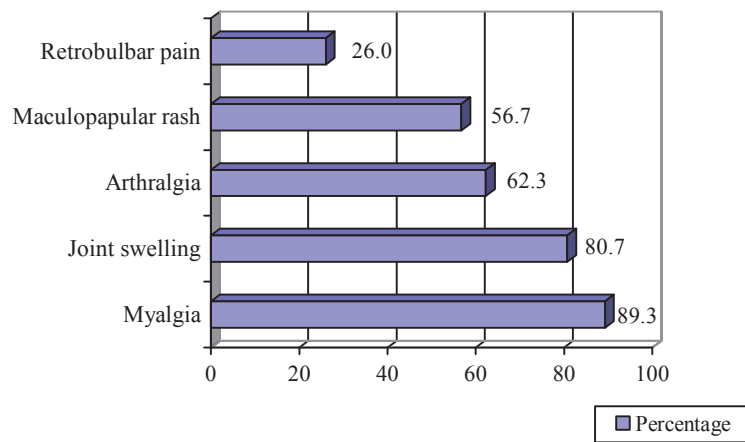


Figure 1. Chief complaints causing 309 patients to seek health care, 2008-2009.

and 1.0% had no symptoms. Of the 405 patients who had completed fever data, 76.0% had high fever, 20.0% had low fever, and 4.0% had no fever. Of the 404 patients who had completed joint swelling data, 69.0% had severe to very severe swelling and 7.7% had no swelling. Of the 391 patients who had completed headache data, 42.7% had moderate headache and 36.8% had severe to very severe headache. Of the 269 patients who had completed arthralgia data, 76.6% had severe to very severe pain and 7.8% had no pain (Table 1).

3. Self-care

The median days of illness before seeking health care was 2 (range, 0 to 60 days) among the 421 patients. Every patient was treated either by health personnel or themselves. Few patients took care of themselves. The majority sought care from health workers, physicians, clinics, folk medicine, or drug stores (mostly analgesic drugs).

The frequency of seeking health care during the illness ranged from 1 to at least 5 times. The percentage of patients who sought health care twice, three times, four times, and at least 5 times was 50.8%,

Table 1. Severity of signs and symptoms among 421 patients, 2008-2009

Signs and symptoms	Number of patients	None (%)	Mild (%)	Moderate (%)	Severe (%)	Very severe (%)
Myalgia	408	1.0	3.9	23.3	58.1	23.7
Joint swelling	404	7.7	6.2	17.1	48.5	20.5
Headache	391	8.7	11.8	42.7	32.5	4.3
Rash	273	15.0	7.7	34.1	33.0	10.3
Arthralgia	269	7.8	3.7	11.9	57.6	19.0
Retro-bulbar pain	263	47.9	17.4	22.0	10.7	1.9
Fever	405	4.0	Present			
			96.0			

18.3%, 5.2% and 2.1%, respectively. Less than 2% of the patients used folk medicine each time.

The proportion of patients seeking care from health workers or physicians for the first (n=415), second (n=214), third (n=76), fourth (n=21), and fifth time (n=9) was 62.5%, 86.4%, 92.1%, 90.6%, and 88.9%, respectively.

DISCUSSION

In general, the clinical manifestations include acute and chronic stages. In the acute stage, the infected individual commonly has a sudden onset of fever, rash, and arthralgia.^(4,7,18,31,32) The arthralgia is characteristically severe. Joint swelling is commonly present. The affected joints frequently occur bilaterally and may involve any joint.^(4,8,18,19,31,32) This study found slightly different clinical manifestation results to those of other outbreaks. In Thailand, there were 94, 576 and 331 cases in 3 outbreaks, which took place in Nong Khai, Khon Kaen, and Nakhon Si Thammarat, respectively.^(10,11,18) The majority of cases had a triad of signs and symptoms, which were fever (92-100%), severe arthralgia (80-98%), and rash. However, the proportions of maculopapular rash were slightly different: 21% in Nakhon Si Thammarat, 50% in Nong Khai, and 72% in Khon Kaen. In this study, most patients had myalgia (96.9%), fever (96.2%), joint swelling (96.0%), and headache (92.9%). Rash and arthralgia were present in about 60%. In part, the explanation for these differences was CHIKV strain and severity. The CHIKV strains were not the same in all three outbreaks. The virus genotype that caused the outbreak in late 2008 was from Central-east

Africa, while that of the previous outbreaks was Asian. This isolated genotype was 99-100% related to those from the outbreaks in Singapore in 2008 and India.^(4,21,30) The recent CHIKV epidemic, from which new variants might have evolved, was related to the Central-east African strain.^(17,33)

For reasons relating to the severity of illness, our case detection method differed from that of other studies, which were mainly hospital-based.^(8,19) Although the joint investigation team conducted outbreak investigations in the same district as one in this study, the clinical manifestations were different. The team found 18 suspected cases who had attended hospital and 64 in communities between August 1st and October 7th, 2008. Almost all 82 cases had arthralgia (86.6%), but only 8.5% had myalgia.⁽²⁶⁾ This study, found that most patients had myalgia at 96.9% and arthralgia at 63.9%. In the initial epidemic, the joint investigation team used a case definition based on previous outbreaks in Thailand, which were caused by different strains of the virus.⁽²⁶⁾ In this study, all possible clinical manifestation were investigated, starting with the list of probable cases from health centers, and then tracking relatives and friends of suspected cases who lived nearby. Thus, the patients who participated in this study could describe all signs and symptoms. The investigation team retrieved data from hospitals where severe cases were more likely to occur, and using their definition of active case finding was also more likely to recruit severe cases. In this study, cases were recruited from villages, where a wide range of signs and symptoms were presented. Our in-depth interview among 21 cases, found that predominant signs and symptoms were different. Severe cases had fever, arthralgia, and myalgia in sequence. Mild

to moderate cases had fever, myalgia, and arthralgia in sequence. Patients with mild to moderate signs and symptoms had myalgia predominantly, while severe cases had arthralgia predominantly (data not shown). Thus, the proportion of myalgia was higher than that of arthralgia in this study. It is worth noting that the three most common signs and symptoms were myalgia, fever, and joint swelling, but the three most common complaints that brought patients to seek care were mainly myalgia, joint swelling, and arthralgia. Prevention and control measures have been delayed and insufficient, particularly those adjacent to outbreak areas where cases were detected. One of the reason was difficulty in identifying the first cases in a formerly CHIKV-free area. (Government Document of Office of Disease Prevention and Control 12, Songkla Province. Key to Success and The Best Practice/Bad Practice Workshop, 17-19 June 2009. Rawi Warin resort and spa, Lanta Island, Krabi province, Thailand).^(4,27,28) A more precise case definition was documented by the Epidemiology Bureau, Public Health Ministry.⁽³⁴⁾ This definition may be slightly complicated in practice for villagers or village health volunteers, who have limited clinical background. However, the findings of this study provide useful information for surveillance systems and prevention and control programs. In primary health care units, where a laboratory is not available, it may be useful to include myalgia in the case definition.

There has been no report of death from CHIKV in Thailand.⁽³⁰⁾ However, there have been many reports of severe clinical manifestation such as neurological involvement and death in India, and encephalitis cases in Cambodia.^(13,35,36) CHIKV infection has a low fatality rate and is not severe from a health

care provider's perspective; however, its effects are serious from the infected person's perspective. In this study, it was found that the majority of patients bought analgesic drugs, including steroidal and nonsteroidal anti-inflammatory drugs (data not shown). Long-term usage of these can lead to additional health problems, particularly in infected persons at the chronic stage.

Another study conducted a serosurvey during the same epidemic period in 2008 and found that 34% of people who confirmed positive by RT-PCR (40 out of 117 cases) were asymptomatic (Pisittawoot Ayood, Thonchai Leatvilairatapong, Suwit Thamapalo, *et al.* Risk factors and chikungunya viral setro survey in a village, Yi-gno district, Narathiwat province, October 2008. Government meeting; May 4, 2009; Epidemiology Bureau, Public Health Ministry, Nonthaburi province, Thailand). Another study of sub-clinical infections also reported⁽²²⁾ that mild or asymptomatic cases may not be detected by the surveillance system. The attack rate was underestimated. At the end of 2008, specific populations from affected areas of southern Thailand, such as college students and soldiers, migrated to other regions of Thailand. In addition, tourists also traveled in and out of affected areas.^(4,27,28,38) The vectors found from epidemic areas were *Aedes albopictus* and *Aede aegypti* mosquito species. The CHIKV infection rate among these vectors was 16%. Relative infection rates in *Aedes albopictus* and *Aede aegypti* were 53% and 10%, respectively.⁽³⁹⁾ Furthermore, there were late winters and high levels of rainfall in 2008 and 2009.⁽³⁹⁾ All the above reasons might contribute to the spread of the virus to other susceptible populations. From 1st January to 27th August, 2010, Chikungunya viral infection spread to 30 provinces.

Currently, 1,289 cases with the highest morbidity rate are still in the south of Thailand (13.12 per 100,000 of the population).⁽³⁸⁾ Therefore, intensive and continuous control and prevention programs are needed. Regions adjacent to the outbreak areas should be investigated, and prevention programs implemented as necessary.⁽²⁸⁾

There are some limitations in this study, for example, it was conducted during a reign of terrorism and political unrest in the deep south of Thailand, while the outbreak was spreading rapidly. We obtained information urgently for the government in order to improve control measures. Not all patients in this study had laboratory confirmation of infection because the test is expensive and it not available on a routine basis. However, clinical manifestations during the epidemic were well accepted for diagnosis, particularly those of fever, arthralgia, and rash. In addition, the results of serosurvey conducted occasionally throughout epidemics by the Public Health Ministry showed only the Central-east Africa genotype. Recall bias of signs and symptoms was possible, as in other observational studies. Nevertheless, this might not have affected results greatly because the severity of each sign and symptom was very high. Furthermore, data were collected just a few months after the epidemic started.

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การระบาดของไวรัสชิคุนกุนยาสายพันธุ์ใหม่ครั้งแรกในไทยและ อาการทางคลินิก 2551-2552

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บทคัดย่อ

บทนำ มีการระบาดของโรคชิคุนกุนยา สายพันธุ์ Central-east African ครั้งแรกในประเทศไทย เมื่อ พ.ศ. 2551-2552

วัตถุประสงค์ เพื่ออธิบายถึงลักษณะอาการทางคลินิกและการดูแลตนเองของผู้ป่วย

วิธีการศึกษา เจ้าหน้าที่สาธารณสุขออกสำรวจพื้นที่ระหว่างเดือนกุมภาพันธ์ ถึงเดือนเมษายน พ.ศ. 2551-2552 พบผู้ป่วย 421 ราย ใน 2 จังหวัดภาคใต้ตอนล่าง ซึ่งเป็นจุดเริ่มต้นการระบาด และได้สัมภาษณ์ผู้ป่วย

ผลการศึกษา ผู้ป่วยส่วนใหญ่เป็นเพศหญิง (ร้อยละ 53.2) ค่ามัธยฐานอายุ 36.0 ปี (พิสัย 12-78) มีอาชีพเกษตรกร (ร้อยละ 62.9) มีค่ามัธยฐานระยะเวลาการเจ็บป่วย 8 วัน พบว่าส่วนใหญ่มา รักษาเนื่องด้วยอาการสามอันดับแรกคือ ปวดกล้ามเนื้อ (ร้อยละ 89.3) ช้อบวม (ร้อยละ 80.7) และ ปวดข้อ (ร้อยละ 62.3) ส่วนลักษณะอาการทางคลินิกที่พบคือ ปวดกล้ามเนื้อ (ร้อยละ 96.9) มีไข้ (ร้อยละ 96.2) ช้อบวม (ร้อยละ 96.0) ปวดหัว (ร้อยละ 92.9) มีผื่น (ร้อยละ 64.8) และปวดข้อ (ร้อยละ 63.9) ค่ามัธยฐานระยะเวลาการเจ็บป่วยก่อนมารักษา คือ 2 วัน (พิสัย 0-60) ความถี่ของการ ไปรักษามีตั้งแต่ 1 จนถึงอย่างน้อย 5 ครั้ง

ข้อสรุป ผลการศึกษาได้ข้อมูลที่เป็นประโยชน์ต่อระบบเฝ้าระวังและการควบคุมป้องกันโรค สำหรับสถานพยาบาลปฐมภูมิที่ไม่มีบริการตรวจทางห้องปฏิบัติการรองรับนั้น น่าจะนำเอาอาการ ปวดกล้ามเนื้อรวมไว้ในคำนิยามผู้ป่วยด้วย ควรที่จะมีการศึกษาเพิ่มเติมเกี่ยวกับอาการแทรกซ้อน ภูมิคุ้มกันโรค และมาตรการการควบคุมโรค **เชียงใหม่เวชสาร 2554;50(1):1-11.**

คำสำคัญ: โรคชิคุนกุนยา Chikungunya ประเทศไทย ลักษณะอาการทางคลินิก ปวดข้อ ปวดกล้ามเนื้อ การระบาด สายพันธุ์ Central-east African genotype