ELSEVIER

Assessing the Spreading Patterns of Dengue Infection and Chikungunya Fever Outbreaks in Lower Southern Thailand Using a Geographic Information System

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PURPOSE: The aims of this study were to assess the incidence of dengue infection (DEN) and chikungunya fever (CHIK) and determine the direction and speed of CHIK between August 2008 and June 2009 in lower southern Thailand.

METHODS: The National Communicable Disease Surveillance System database and a geographic information system containing data on case locations were combined. R and ArcView were used for identifying incidence, direction, and speed of disease outbreaks.

RESULTS: A total of 27,166 patients were identified, of which 3,319 and 23,847 had DEN and CHIK, with incidences of 73 and 521 per 100,000, respectively. The direction of the CHIK outbreak moved from south to north with a median speed of 7.5 km per week. CHIK cases increased after 6 weeks of increasing cumulative rainfall with variation of average daily temperatures (23.7−30.7°C) per week. There was no clear association of DEN with climate variables.

CONCLUSIONS: The combination of surveillance and geographic information system data of DEN and CHIK can be used to determine the speed and direction of disease spread. DEN is endemic, but CHIK is an emerging disease. Because of the rapid spread of CHIK, strict and timely integrated vector control programs after case notification must be implemented.

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KEY WORDS: Chikungunya fever, Dengue, Geographic Information System, Lower Southern Thailand, Outbreak.

INTRODUCTION

Dengue infection (DEN) and chikungunya fever (CHIK) are mosquito-borne diseases which are important to the public health in tropical and subtropical countries (1, 2). The common vector of DEN is *Aedes aegypti*, whereas for CHIK are *A. aegypti* and *Aedes albopictus*.

DEN and CHIK are transmitted by the *Aedes* mosquito; however, the epidemiology and clinical presentations are different (3–6).

The epidemiology of DEN is endemic in tropical and subtropical areas; in contrast, CHIK is a reemerging disease. The first case notification of DEN in the world was inconclusive (7), whereas the first outbreak of dengue hemorrhagic fever (DHF) was reported in the Philippines in 1953 before it spread throughout southeast Asia (8). For CHIK, the first outbreak was reported in Tanzania in 1952−1953 (5, 6, 9), from there, it spread around the world from Africa to Asia and to Europe in 2007 (5, 9–11). In southeast Asia, DEN is hyperendemic, but CHIK is reemerging and unpredictable (9, 12). In Thailand, DEN and CHIK outbreaks were first reported in Bangkok in 1958 and then 1976, 1988, 1991−1993, 1995 and disappeared until 2008 (3, 8, 13–15). DEN and CHIK occurred simultaneously in Thailand in 2008–2009 (16, 17).

The clinical spectrum of DEN is varied, as dengue fever (DF), DHF, or dengue shock syndrome (DSS) (1). DEN shares some clinical signs and symptoms with CHIK (5, 14, 15), but it is less severe. People infected with CHIK suffer from joint pain, and more than 12% will develop chronic joint symptoms leading to poor quality of life (4, 5, 18). Fifty million people worldwide are affected by DEN every year, of which 2.5% have died with DHF (19). Likewise, DEN is a high-burden disease in Thailand, causing 95 deaths in 2007 (16). In 2002, the disability-adjusted life years for DEN was 230.6 per million (20).

Geographic information system (GIS), which is a special information system containing spatial data (raster and

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Selected Abbreviations and Acronyms

DEN = dengue infection
CHIK = chikungunya fever
DHF = dengue hemorrhagic fever
DF = dengue fever
DSS = dengue shock syndrome
GIS = geographic information system
UTM = Universal Transverse Mercator

vector) and attribute data (character and numeric), can provide an accurate measure of distances and areas (21, 22). Previous studies in which the authors used GIS as a tool for analyzing geographic patterns of vector-borne diseases were the spatial distribution of DEN virus-infected *Aedes* mosquito (23), space-time analysis of dengue cases (24), climatic conditions for *Aedes* infestation (25), and factors associating with vector-borne disease transmission (23, 26, 27).

In Thailand, the disease surveillance data has also shown that DEN is an endemic disease and that CHIK is a reemerging disease, with the last CHIK patient reported in 1995 (15, 28). In 2008, the first CHIK patient was notified in the Narathiwat province, in the deep south of Thailand (29). DEN spread widely across the country, with the highest morbidity found in the southern provinces. In 2007, the morbidity was 138 per 100,000 population (16).

Although a disease surveillance database is available, there is a lack of studies on the spreading patterns, including incidence, direction, and speed of DEN and CHIK. Understanding the spread and pattern is necessary for successful disease control and improving the use of surveillance data. The aims of this study were thus to assess the incidence of DEN and CHIK outbreaks and determine the direction and speed of CHIK in lower southern Thailand.

METHODS

Study Design and Setting

A descriptive study was conducted in the lower south of Thailand, in seven provinces, namely Narathiwat, Pattani, Yala, Songkhla, Trang, Phatthalung, and Satun from June 2009 to May 2010. This study was approved by the Institute Ethical Committee of Faculty of Medicine, Prince of Songkla University with document reference 52-263-18-5-3-1.

Data Sources

Two data sets, including the National Communicable Disease Surveillance System database from the Office of Disease Prevention and Control 12, Songkhla and GIS, database were used. DEN, which includes DF, DHF, and DSS, and CHIK cases diagnosed between August 10, 2008, and June 13, 2009, were retrieved from the National Communicable Disease Surveillance System database. All cases reported in this database include the status of suspected, probable, and confirmed cases. Suspected cases were defined by clinical criteria that define DF as acute fever with at least two manifestations (headache, retro-orbital pain, myalgia, rash, hemorrhagic); DHF as hemorrhagic by a positive tourniquet, bleeding, or plasma leakage; DSS as DHF grade III and IV in which shock is evident; and CHIK as high fever with rash and joint pain. Probable cases were suspected cases that confirm with the use of basic laboratory tests, with DF defined as a white blood cell <5000 cells/mm^3 with high proportion of lymphocytes; DHF as a platelet count $<100{,}000$ cells/mm^3, hemoconcentration (10%−20% increasing), or pleural effusion; DSS as narrowing of pulse pressure, and CHIK as low white blood cells and epidemiological criteria (i.e., visited epidemic area within 15 days). Confirmed cases were probable cases that define with specific laboratory tests such as virus isolation, immunoglobulin M antibodies, or a fourfold increase in immunoglobulin G titers (30–32). However, there is no specific code to differentiate this status, so a subgroup analysis was not possible.

Demographic data (age, sex, and area of residence), place of treatment, admission status, and geographic location of each case from this National Communicable Disease Surveillance System database was extracted (33, 34). Area of residence in this database is classified as municipality (residence in a community having >5000 population), rural (residence in a community having <5000 population) or unidentified. Place of treatment is classified as tertiary hospital (hospital having >500 in-patient beds with specialists), general hospital (hospital having 200–500 inpatient beds with specialists), community hospital (hospital having 10−150 inpatient beds), and health care center (outpatient only). For each case, the date of onset was transformed as the number of weeks since August 10, 2008. The location of each case was recorded as their village of residence, defined by the Ministry of Interior (33). In addition, daily climatic factors, namely rainfall (mm) and temperature (°C) were obtained from the South Western Metrological Center, Phuket and South Eastern Meteorological Center, Songkhla, Thai Meteorological Department, Ministry of Information and Communication Technology.

The Universal Transverse Mercater (UTM) coordinate system was used for geographic data. The GIS database (in shape file format) from the Geo-Informatics Research Center for Natural Resource and Environment, Prince of Songkla University, was applied. For the location of Thailand, we used the UTM projection zone 47N (22), and the specific X- and Y-coordinate for each village was then constructed by use of the Arc View GIS program (35). Two data sets were merged with the village code as a common field.

Outcome Variables

Spreading pattern of disease was classified as incidence, direction, and speed. Incidence of DEN and CHIK was presented in terms of the number of new cases each week and cumulative incidence by province. Direction of CHIK spread was considered by two methods: a movable location of new cases occurring each month and a movable location of centroid (average of X- and Y-coordinate) of new cases occurring each week. Speed of CHIK spread was determined by an average distance (kilometer) from each centroid of cases divided by time (week).

Data Analysis

Statistical analysis was performed by the use of R software version 2.10.1 (36) and ArcView GIS (35). The differences of demographic characteristics among DEN and CHIK cases were analyzed by rank sum test or chi-square test as appropriate. The variation of incidence of DEN and CHIK was tested by trend analysis using a linear regression model with quadratic term. The association between incidence of CHIK and climatic factors, rainfall, and temperature was descriptive.

The centroid was calculated by averaging the X- and Y-coordinates of all new cases within the same week. To determine speed, the distance between each village was calculated as a formula: $\sqrt{(Xi - Xo)^2 + (Yi - Yo)^2}$, where X_0 and Y_0 are the X and Y coordinates of the current week and Xi and Yi are the X and Y coordination of the following week.

RESULTS

During the study period, 27,166 patients were identified, of which 3,319 and 23,847 cases were DEN and CHIK, respectively (Table 1). Of those with DEN, 1447 (43.6%) and 1827 (55.0%) were DF and DHF, respectively. A total of 45 DEN cases were diagnosed as DSS, and of these, 3 cases died. The mean age of patients who were diagnosed with CHIK was greater than for DEN, and 53.5% of DEN cases were male whereas 58.9% of CHIK cases were female. Most of DEN (85.5%) and CHIK (86.5%) patients lived in rural areas. Most CHIK patients (78.9%) visited community hospitals, but 42.3% and 33.9% of DEN cases were treated at community and general hospitals. 75.4% of DEN cases were admitted, whereas 92.9% of CHIK cases were treated as outpatients. Age, sex, place of treatment, and admission of DEN and CHIK were significantly different.

The incidence of DEN and CHIK in each week during the study period ranged from 2 to 118 and 1 to 1659 cases, respectively. We found that the incidence of DEN in each week was fairly constant throughout the period of study (Fig. 1A). This was supported by a test for trend using linear and quadratic terms with p-values .17 and .4, respectively. The incidence of CHIK was bimodal (Fig. 1B); the first peak occurring during January 25 to 31, 2009, and the second peak from April 25 to May 2, 2009. The overall

TABLE 1. Characteristics of DEN and CHIK patients

	DEN					
	DF	DHF	DSS	Total	CHIK	
Characteristic	n = 1,447 (%)	n = 1,827 (%)	n = 45 (%)	n = 3,319 (%)	n = 23,847 (%)	p value
Age (mean ± SD) year	19.4 ± 15.8	18.9 ± 14.7	19.1 ± 19.2	19.2 ± 15.3	35.4 ± 18.6	<.001
Sex						
Male	783 (54.1)	971 (53.2)	20 (44.4)	1,174 (53.5)	9,796 (41.1)	.04
Female	664 (45.9)	856 (46.8)	25 (55.6)	1,545 (46.5)	14,051 (58.9)	
Area of residence						
Municipality	157 (10.9)	186 (10.2)	7 (15.6)	350 (10.6)	2,284 (9.6)	.20
Rural	1,230 (85.0)	1,573 (86.1)	34 (75.6)	2,837 (85.5)	20,614 (86.5)	
Unidentified	60 (4.1)	68 (3.7)	4 (8.8)	132 (3.9)	949 (3.9)	
Place of treatment						
Tertiary hospital	204 (14.1)	401 (21.9)	2 (4.4)	607 (18.3)	1,128 (4.7)	<.001
General hospital	486 (33.6)	617 (33.8)	23 (51.2)	1,126 (33.9)	1,143 (4.8)	
Community hospital	667 (46.1)	718 (39.3)	18 (40.0)	1,403 (42.3)	18,827 (78.9)	
Health care centre	4 (0.3)	7 (0.4)	0	11 (0.3)	1,460 (6.1)	
Private hospital	86 (5.9)	84 (4.6)	2 (4.4)	172 (5.2)	1,289 (5.4)	
Patient type						
Nonadmitted	449 (31.0)	351 (19.2)	15 (33.3)	815 (24.6)	22,156 (92.9)	<.001
Admitted	998 (69.0)	1,476 (80.8)	30 (66.7)	2,504 (75.4)	1,691 (7.1)	

DEN = dengue infection; CHIK = chikungunya fever; DF = dengue fever; DHF = dengue hemorrhagic fever; DSS = dengue shock syndrome.

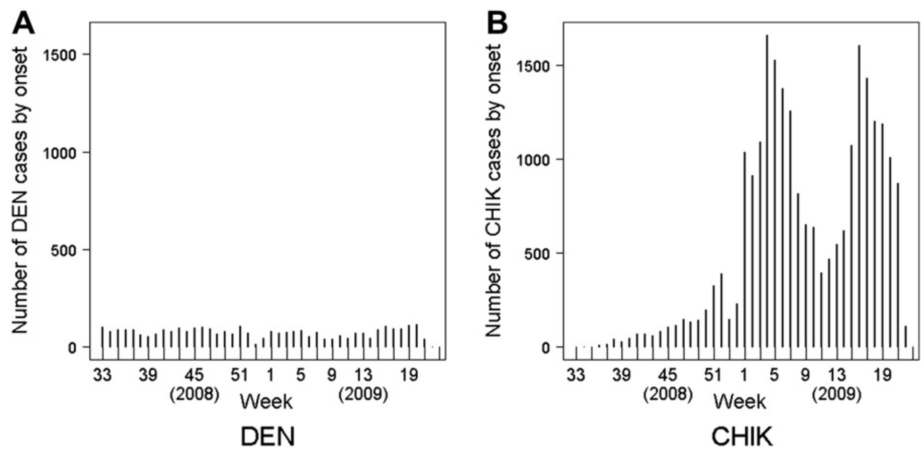

FIGURE 1. Weekly incidence of DEN (A) and CHIK (B) between August 2008 and June 2009.

incidence of CHIK and DEN was 521 and 73 per 100,000 population, respectively. The greatest incidence of DEN (104.2 per 100,000 population) occurred in Songkhla province (Fig. 2A), whereas the greatest incidence of CHIK (1,147.5 per 100,000 population) occurred in Narathiwat province (Fig. 2B).

An association between climate variables and disease incidence was observed (Fig. 3). Narathiwat, Pattani, Yala, Songkhla, Trang, and Phatthalung provinces clearly showed that after the 6 weeks of increased cumulative rainfall, there was a sudden increase in the incidence of CHIK. There was no clear association of temperature with CHIK. There was no clear association of DEN with climate variables. Average rainfall was 53.6 mm per week, ranging from 0 to 699.7 mm. Average temperature was 27.3°C with variation in temperature (23.7−30.7°C) during the 44-week period was noted throughout the region.

The directions of new cases at four-week intervals using X- and Y-coordinates are shown (Fig. 4). Initially, CHIK cases occurred in Narathiwat province, the southernmost province of Thailand bordering Malaysia (Fig. 4A-B). Cases then moved north (Songkhla and Pattani; Fig. 4C-D), then south (Yala) before moving north again along the peninsula (Fig. 4E-K). A centroid plot shown in Figure 5 also shows that the outbreak moved from the south to the north of the peninsula. During the study period of 44 weeks, a total distance of 484 km was covered by the CHIK outbreak. The median speed of CHIK was 7.5 km per week, ranging from 1.2 to 57.4 km per week.

DISCUSSION

The incidence, direction, and speed of CHIK and incidence of DEN were retrieved effectively by use of data in both the National Communicable Disease Surveillance System database and the GIS database. Although CHIK was emergent in lower southern Thailand in 2008, its incidence was greater than that of DEN. The specific direction and rate of spread of CHIK was also identified.

Our study found that the incidence of CHIK (521 per 100,000 population) was seven times greater than DEN (73 per 100,000 population). Data on incidence of CHIK cases from the last emergence in 1995 were 1001 (15). The incidence of DEN varied from 44.4 per 100,000 population in 2006 to 151.9 per 100,000 population in 2007. This finding may be explained by herd immunity as the result of different strains of emerging CHIK and vector competition with different life expectancy and flight radius of vectors (2, 5, 14, 37, 38).

The recent emerging CHIK outbreak in Thailand was caused by the “Central/ East African” strain and was different from the previous “Asian” strain (14, 39) and a mutation of E1 226V of “Central/ East African” (39) strain. This can lead to a lack of herd immunity in the population. It is likely the main factor that influences the incidence of CHIK. There is evidence that an absence of a virus circulating in a community can lead to an explosive outbreak (40). *A. aegypti*, the main vector for DEN, prefers crowded, urban areas, and so predominates over *A. albopictus* in urban areas (41). Both *A. aegypti and A. albopictus* compete in terms of the same blood sources (42–44) and larval habitats (45). In the absence of *A. aegypti* in urban habitats, *A. albopictus* may colonize instead (46). In addition, *A. albopictus* has a relatively longer life expectancy and average distance of flight radius compared with *A. aegypti* (5, 37).

In our study, DEN and CHIK were commonly detected in rural areas, similar to a previous study in Thailand (15, 47). We found that DEN was common in young adults (19 years old), although CHIK was common in adults (35 years old). In 1995, in Thailand, CHIK patients were between 10–64 years of age, which similar to Indonesia

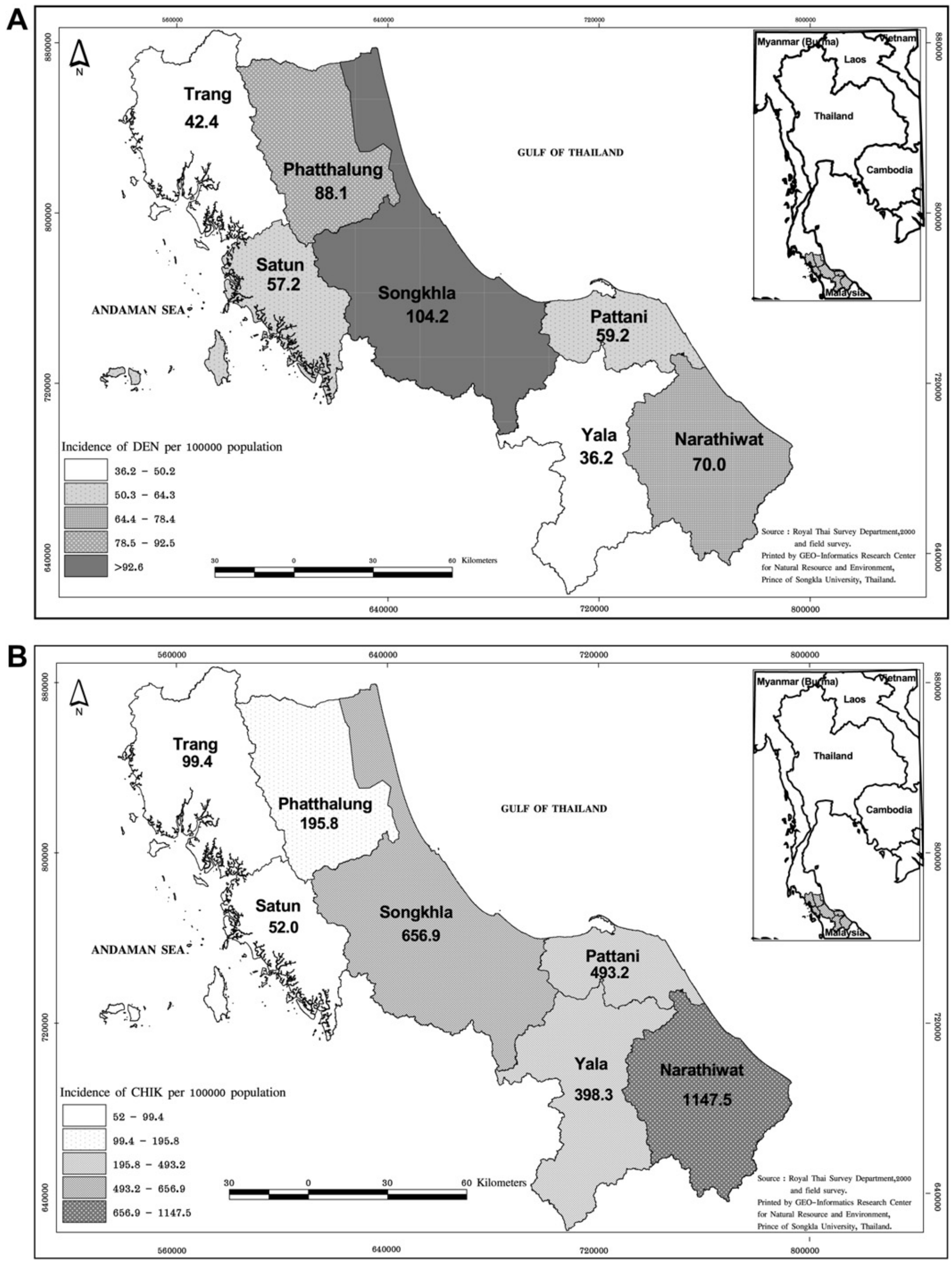

FIGURE 2. A shade plot showing incidence of (A) DEN and (B) CHIK (per 100,000) by province.

and Italy (10, 15, 48). The greatest risk group of DEN was 5- to 9-year-old children (47, 49, 50). We found that CHIK was more common in women compared with DEN, a result similar to previous studies (10, 14, 49).

We were able to determine the direction and speed of spread for CHIK by combining the National Communicable Disease Surveillance System database with GIS data. The index case of CHIK in our study was reported in Narathiwat province in August 2008 and moved northward in our study. This finding might be attributable to the geographic characteristics of southern Thailand being located on a peninsula and the migration or traveling of lower southern people to the cities at the upper part of the peninsula. The authors of previous studies in Malaysia and Italy described that the

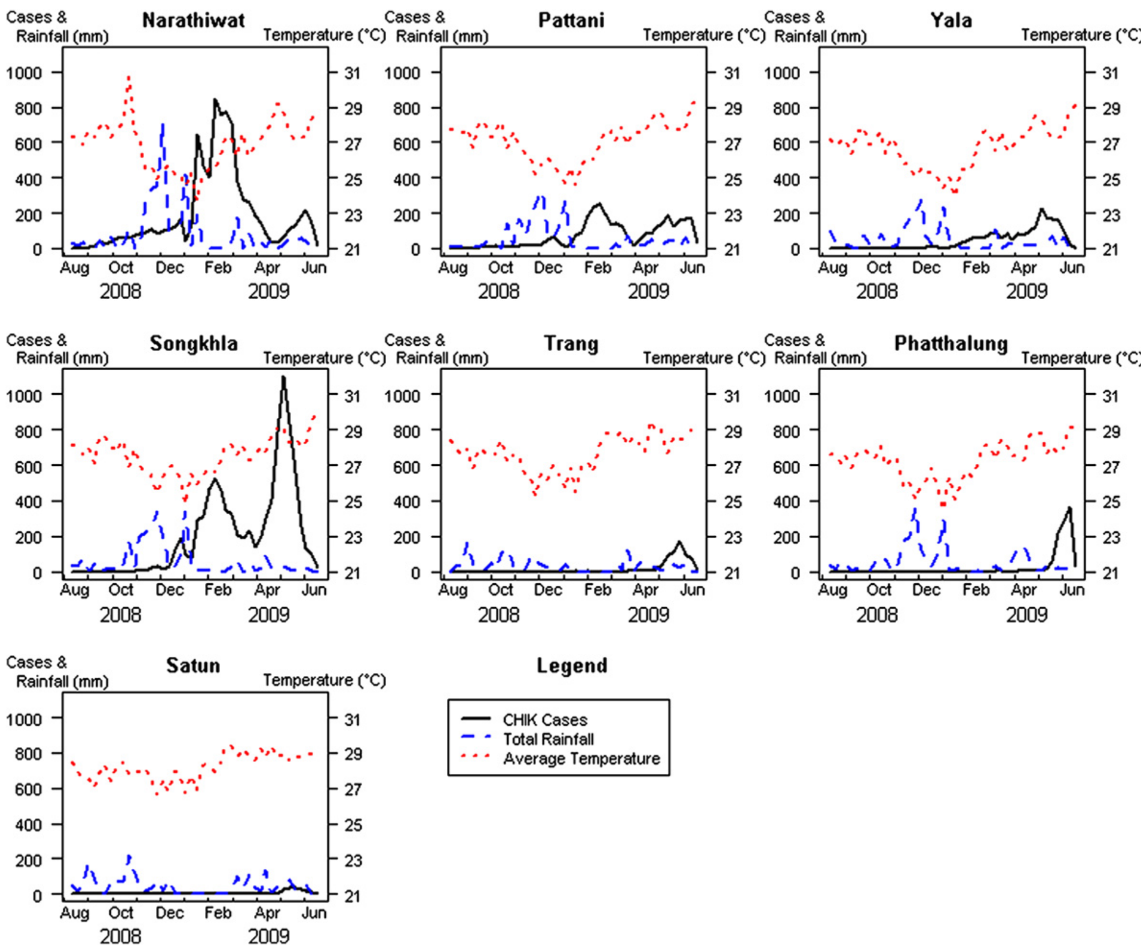

FIGURE 3. The association between climate variables and CHIK incidence between August 2008 and June 2009.

spread of CHIK depended on the population traveling, household density, and population density (5, 10, 51). Narathiwat province is the southernmost province of Thailand bordering Malaysia and data outside Thailand was not available. However, study reports that the outbreak of CHIK were established in Singapore and Malaysia before moving to Thailand (51, 52).

Climatic variables (cumulative rainfall and average temperature per week) were not clearly associated with DEN cases in our study because of the small number of cases and constant incidence per week. Also, we did not have enough data on CHIK cases to perform a detailed time series analysis. Previous authors found that the ecologies of mosquito borne disease can be complex and difficult to predict, and more climate variables are needed to make a more detailed assessment (53). DEN and CHIK outbreaks occurred in rainy season same as previous in Thailand, Indonesia (15, 48). High rainfall or temperatures can increase DEN and CHIK transmission likewise, drought can also participate a role if household water storages increase the number of mosquito breeding sites (54).

Strengths and Limitations

This study demonstrated the advantage of incorporating the UTM coordinate system in GIS into the National Communicable Disease Surveillance System database to define the incidence, direction, and speed of diseases. There have been no previous studies in which the authors demonstrate the incidence of both DEN and CHIK occurring in the same place and time since this is the first time that the "Central/East African" strain of CHIK has appeared in Thailand.

This analytic and decision making tool using the incidence of cases in the same week from National Communicable Disease Surveillance System database and the coordinates of incidence cases from GIS can provide the centroid of case representative resulting distance of spread, direction and speed to set up appropriate timing of control program and potential risky areas.

There were a few limitations of our study. First, the application of the centroid as the average X-and Y-coordinate in each week may inflate the point of incidence cases. For CHIK, the incidence of index case was notified explicitly

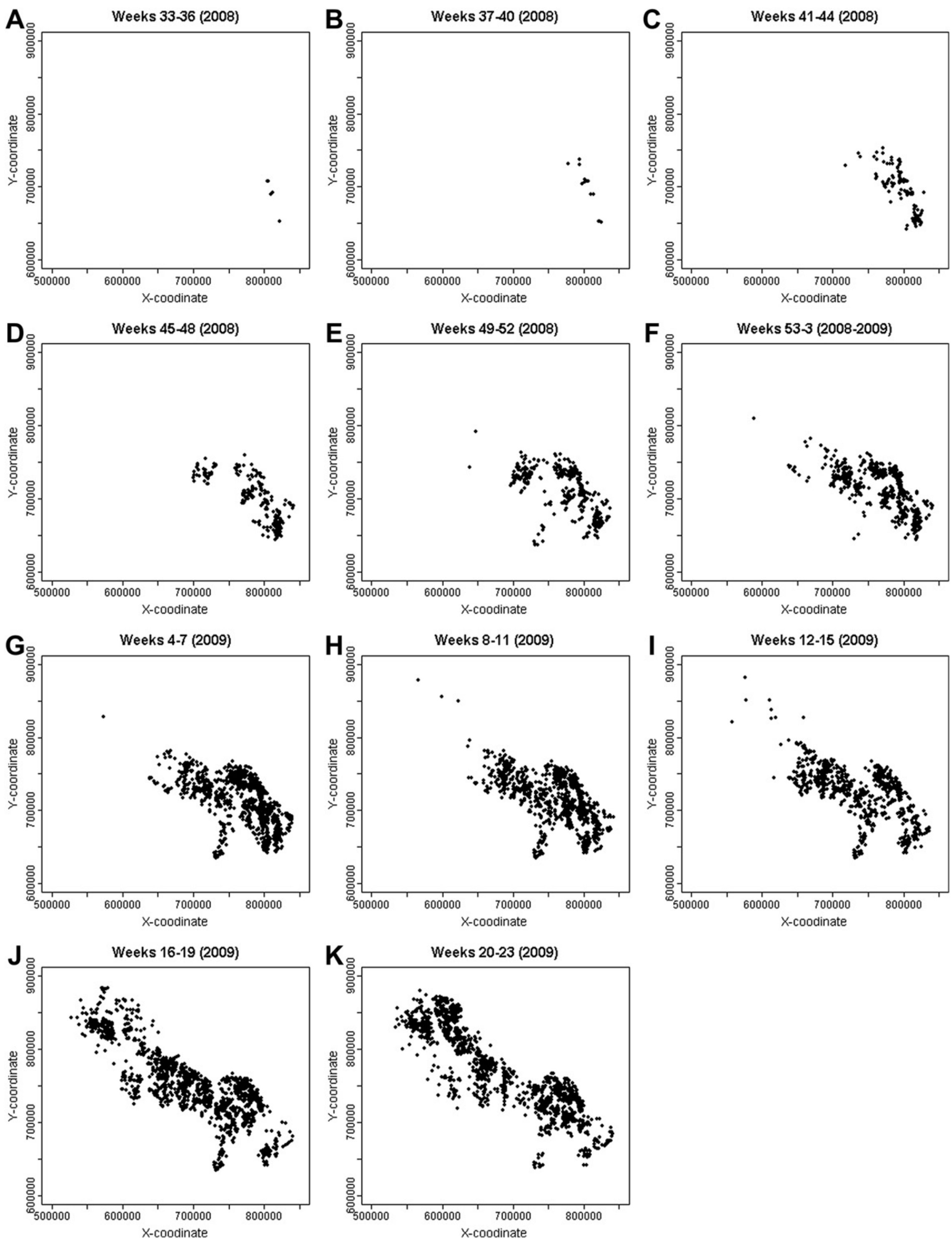

FIGURE 4. Scatter plot of cumulative numbers of CHIK cases by month during August to December 2008 (A-F) and January to June 2009 (F-K).

within the province and the centroid of each week provided the specific direction. In contrast, 105 index cases of DEN were notified in multiple provinces in the same week. Although the centroid of DEN could be calculated, the disperse direction of DEN was shown. This finding might be attributable to an endemic pattern of DEN. For this

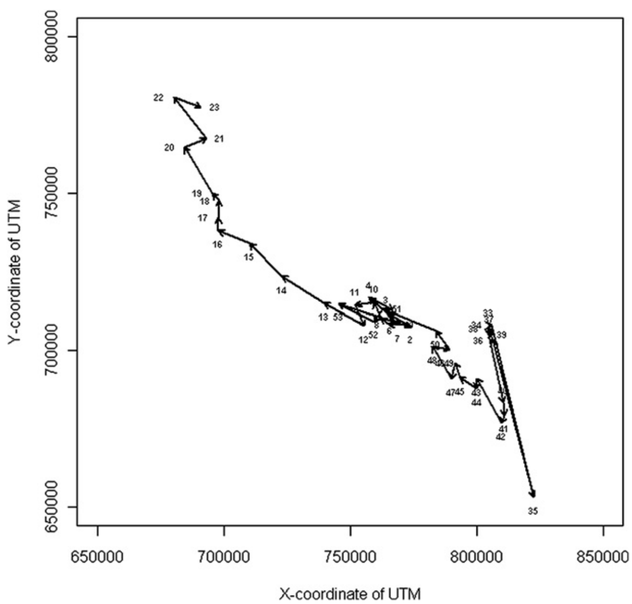

FIGURE 5. Direction of spread of CHIK by week (2008–2009) in lower southern Thailand.

reason, the direction and speed of DEN was not assessed in this study. Secondly, the study setting was a peninsula, thus movement of the population may be limited from the south to the north. Further studies that use the combination of surveillance and GIS data of CHIK in different areas are needed to confirm the reproducibility of direction and speed of this disease.

CONCLUSIONS

The combination of National Communicable Disease Surveillance System database of CHIK and DEN and GIS data can be used to determine the speed and direction of disease spread. DEN is endemic, but CHIK is an emerging disease. Because of the rapid spread of CHIK, strict and timely integrated vector control programs after case notification must be implemented.

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