Epidemiological characteristics and determination of spatio-temporal clusters during the 2013 dengue outbreak in Chiang Mai, Thailand

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Abstract

Dengue is the worldwide most important mosquito-borne viral disease in humans. A large dengue outbreak occurred in Chiang Mai, Thailand in 2013. The aims of this study were to describe the epidemiology of this outbreak and determine the spatio-temporal pattern in the sub-district with the highest number of dengue cases. Data on patients, including date of illness, were obtained from the Chiang Mai Provincial Public Health Center and analyzed descriptively using R statistical software. The geographic location of patients' residences was determined from available geographical information databases supplemented with coordinated data collection in the field. A space-time permutation model from SaTScan™ was used to determine disease clusters corresponding to space and time. Results showed that Muang District, the centre of the province, had a higher number of cases than the other 25 districts. The Suthep subdistrict, part of Muang District, had most of the patients: 625 subjects distributed between 213 res-

idences. The space-time analysis identified a primary cluster and 7 secondary clusters in different time periods. The primary cluster had 128 patients in a period of approximately 3 months. The number of patients in the secondary clusters ranged between 7 and 65. Most of the clusters occurred in densely populated areas during June and July (the rainy season). The finding from this study may support health agencies to plan surveillance campaigns for people at specified local areas with a high incidence of the disease.

Introduction

Dengue is a global arboreal disease affecting humans primarily through transmission by the *Aedes aegypti* mosquito. The disease represents a significant socioeconomic and health burden in at least 100 countries in all regions of the world, particularly those with warm tropical climates (Guzman and Kouri, 2002; Gubler, 2011). The World Health Organization (WHO) estimates that more than 3.9 billion people are at risk for the disease globally, that 390 million people are actually infected (WHO, 2020). There were 1.3 billion at-risk individuals in ten dengue endemic countries in South-East Asia (SEA), where dengue is a leading reason for hospitalization and sometimes death in children (WHO, 2012). Severe dengue is endemic in most SEA countries, with infection rates 18 times higher than in the Americas (Ferreira, 2012; WHO, 2012; Shepard *et al.*, 2013). According to dengue surveillance data from the Thai Ministry of Public Health (MOPH) in 2013 there were 154 444 reported cases of dengue infection in Thailand with 136 deaths nationwide. According to the MOPH's Bureau of Vector Borne Diseases (BVBD), morbidity and mortality rates in 2013 were 241.0 and 0.2 per 100 000 population, respectively (BVBD, 2013). A more recent report shows that there are now 102 553 cases with a morbidity rate of 154.7 per 100 000 people (BVBD, 2019).

Seasonality has been mentioned as an important factor. A systematic literature review of epidemiological trends of dengue in Thailand indicates a heterogeneous, geographical pattern with the incidence of Dengue Fever (DF) varying in both space and time (Limkittikul *et al.*, 2014; Mohd-Zaki *et al.*, 2014). One of the largest outbreaks in Thailand occurred in Chiang Mai Province in 2013. According to the Chiang Mai Provincial Public Health Office (CMPPHO), this area had 11 463 cases in 2013, most of whom in the central district Muang of the capital city of the Chiang Mai Province. With 2 260 cases, 2 032 of whom were Thais and 228 foreigners, the Muang District had the highest dengue morbidity incidence (CMPPHO, 2013) in the area. The complexity of the dengue problem is related to several factors

including the general behaviour of the vector and its relationship with environmental climate variables, temperature in particular, that affects the density of breeding sites. In addition, vector control efforts, urbanization, human population density and population movements all play important roles in this respect. Despite many epidemiological reports, *e.g.*, Barbazan *et al.* (2002) and Wongkoon *et al.* (2013), advanced epidemiology reports using spatial analysis methods are less common.

The residence of patients plays an important role in epidemiology and Geographical Information Systems (GIS) and spatial statistics offer a highly effective tool for determining patterns of disease. This can be done by space only, by time only or by space and time simultaneously. Spatial and space-time scan statistics are the main tools in geographic disease surveillance for investigating if data are randomly distributed clustered. The SaTScan™ software, based on the work by Kulldorff *et al.* (1997), is designed to detect spatial, temporal and space-time disease clusters. There are four types of retrospective analysis: purely spatial, purely temporal, space-time and spatial variation in temporal trends. A space-time permutation model can be used when only information about the spatial location and time of each case is available but where there is no information about the number of controls in case-control studies or the size of the population at risk.

Although several new studies have been published on the spatial epidemiology of dengue in Thailand (Phanitchat *et al.*, 2019; Xu *et al*., 2019), data from particular local areas with high incidence of dengue using spatial models are very limited. One of the studies mentioned demonstrates the use of spatiotemporal analysis to determine spatial and temporal pattern of dengue incidence providing more understanding in epidemiology of the disease (Phanitchat *et al.*, 2019). However, the highest data resolution was limited to the sub-district level. For a better approach to disease prevention and control, local cluster analysis in areas with a high incidence of dengue should be carried out.

While traditional epidemiological procedures based on the number of cases and the time period provide limited results, a spatio-temporal model allows greater evaluation of both magnitude and severity of an outbreak (Wen *et al.*, 2006). Lack of space and time information limits the understanding of the dynamic pattern of dengue at the local scale that might help identify the outbreak mechanism. For that reason, this study analyzed dengue outbreak data retrospectively using a space-time model to identify clusters of disease in a high-risk area with the aim to describe and analyse dengue outbreak data using a general epidemiology approach and the space-time model. This study is the first report on the household level for an analysis of spatio-temporal dengue outbreak clusters in northern Thailand.

Materials and methods

GIS data collection was performed in the field at the sub-district level. We used official provincial dengue outbreak data and geographical data to construct space-time models. The process started with analyzing outbreak data at the district level to determine which district had the highest number of dengue cases followed by identification of the sub-district with the same criteria.

Study area

Chiang Mai, the largest province in northern Thailand, consists

of 25 districts, 204 sub-districts and 2 066 villages located about 300 m above the mean sea level around geographical coordinates 18°47'46.1148''N and 98°58'45.3468''E (Figure 1). It has a total area of 20,107 km^2 and a population of about 1.6 million, around 54% of which consisting of children and teenagers. The centre of Chiang Mai consists of the Muang District, which is composed of one city municipality, one town municipality and 8 sub-district municipalities. It has a large population and is an important location for administration, economic activity, education and tourism.

The annual mean temperature is 22-29°C and the rainy season starts in May and lasts through October. The annual rainfall averages 1,098 mm (40 inches), most of which falls during the rainy season. August is the wettest month, with an average of 226 mm. Between January and March there are only traces of precipitation.

Data collection

Dengue hospital data

In 1980, the National Surveillance System under the Bureau of Epidemiology, Ministry of Public Health, constructed a reporting system for dengue. Initially, all people who visited hospitals with specific symptoms (temperature ≥38°C, headache, arthralgia, and myalgia) were suspected of dengue infection and examined further to confirm the infection. It is important to note that all dengue cases were diagnosed by trained physicians using the WHO case
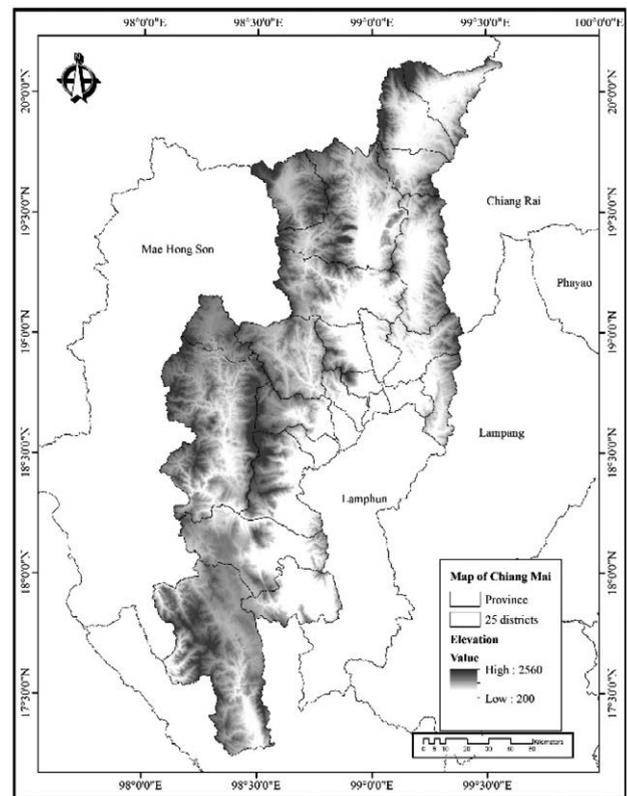
Figure 1. The study area: Chiang Mai Province, Thailand.

definition (WHO, 2017). It is mandatory to report all confirmed cases to the National Surveillance System (Sudjaritruk, 2011). Information on patients (name, age, sex, day of onset and address where the case occurred) was initially recorded using a specific form (Form 506), which is used by all government hospitals and some private hospitals in the province to send the data electronically to CMPPHO. For this study, we obtained a subset of CMPPHO data with personal patient information, such as name, age and sex, excluded due to ethical reasons.

Geographical data

The main focus of the space-time analysis was the occurrence of dengue in 2013 in the sub-district with the highest total number of dengue cases. Since the hospital data do not contain specific geographical data, we collected the coordinates of the patient residences from a satellite map and conducted a field GIS-supported collection without interfacing with any patients directly. All geographical coordinates under field work was collected using a Global Positioning System (GPS) receiver and transferred to a microcomputer using the Quantum GIS computer program (QGIS, 2016).

Descriptive statistics and disease mapping

Data were manipulated and subjected to descriptive statistics according to R Core Team (2017). We calculated the total number of cases stratified by district and morbidity rate per 100,000 populations. A 2013 map of Chiang Mai was used as a reference for morbidity rates of dengue using QGIS.

Space-time analysis

Data used for the space-time permutation analysis consisted of i) geographical coordinates of residences (Universal Transverse Mercator (UTM) zone 47N); ii) date of illness; and iii) the number of cases. The analysis was done with space-time permutation from SaTScan™ version 9.4.2 (Kulldorff, 2017). The space-time model in SaTScan™ was used to identify clusters of disease cases strongly related in place and time as of the date of the analysis (Kulldorff, 2001). We analyzed the dengue case distribution by collecting the individual residence locations and noting the time period for each patient. The dengue dataset used thus consisted of the date of illness and the geographical coordinates for each patient residence which also showed the total number of patients at that location.

Space-time cluster analysis provides a window across space and time allowing the number of observed and expected cases to be counted. In this way, the characteristics of significant clusters can be assessed for statistical significance. The SaTScan™ detects space-time clusters by using circular geographic windows and time intervals expressed as the height of a cylinder with the window as base. The programme evaluates a set of cylindrical windows by considering all those spatially centred at any given point on a user-specified grid and repeatedly varying the cylinder radius and the time duration. For this study, the period of the study was set at 365 days (January through December 2013) with a time aggregation unit of 1 day. The maximum size of the window for spatial clustering was defined to include 50% of the population at risk. This is the recommended value to avoid bias, since larger windows would indicate exceptionally low rates outside the circle and thus make readings less reliable (Kulldorff, 2017). The maximum time was set as 50% of the study period. A likelihood ratio was calculated for each space-time window to test the null hypothesis (that the rate is the same inside as outside the window) against the alterna-

tive hypothesis (that there is an elevated event rate within the window). The distribution and statistical significance of clusters was explored by means of Monte Carlo replication of the data sets under the null hypothesis with 999 replications to ensure adequate power for defining presumptive clusters. The excess of observed cases was noted and its statistical significance evaluated taking into account multiple testing with reference to the many potential cluster locations and sizes evaluated (Kulldorff, 2001).

Results

Descriptive statistics

Dengue cases occurred in all districts of Chiang Mai Province, even in rural areas where there was a low density of villages and population. The five districts (out of a total of 25) with the highest dengue morbidity rate were Mae Ai, Hang Dong, Mae Tang, San Sai and Muang (Figure 2). Although the Mae Ai District, a rural highland area, was identified as the district with the highest morbidity rate for dengue, the highest number of cases was seen in the central Muang District (Figure 3). Its sub-district Suthep had the highest number of dengue cases; interestingly, all 15 villages in this sub-district included dengue cases.
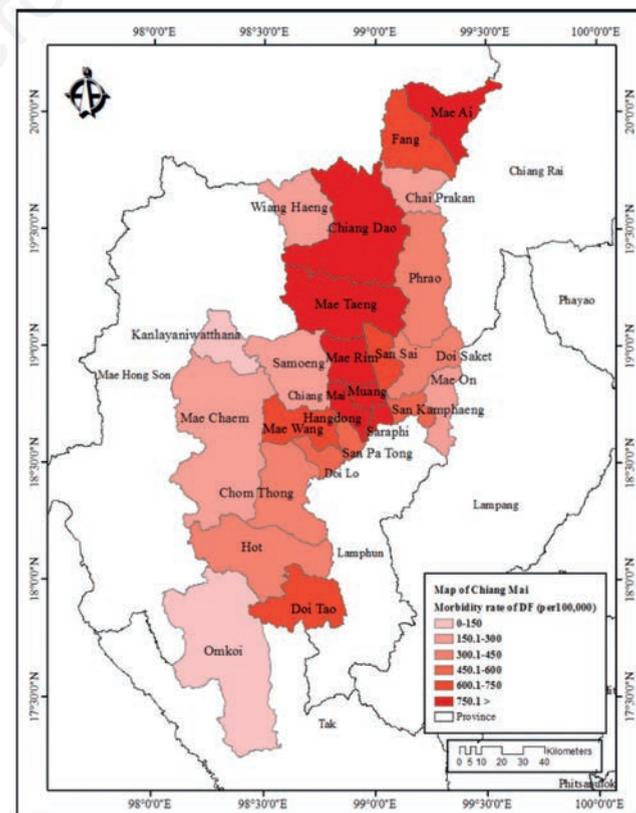
Figure 2. Dengue morbidity rate per 100,000 populations in Chiang Mai Province in 2013.

Cluster detection

In the sub-district of Suthep there were 625 dengue cases at 213 different locations. The space–time test identified 7 significant clusters (Table 1 and Figure 4) in different time periods (days). The primary cluster (Cluster 1) was located exclusively in the Chiang Mai University (CMU) area where dengue cases were identified in the July through September period. Six secondary clusters (Clusters 2-7) were included residences located in 12 community areas: Huay Keow, Paha, Mai Langmor, Wing 41, Suan Dok, Lingha, Umong, Pong Noi, San Lomchoi, Ram Poeng, Sai Kham and CMU.
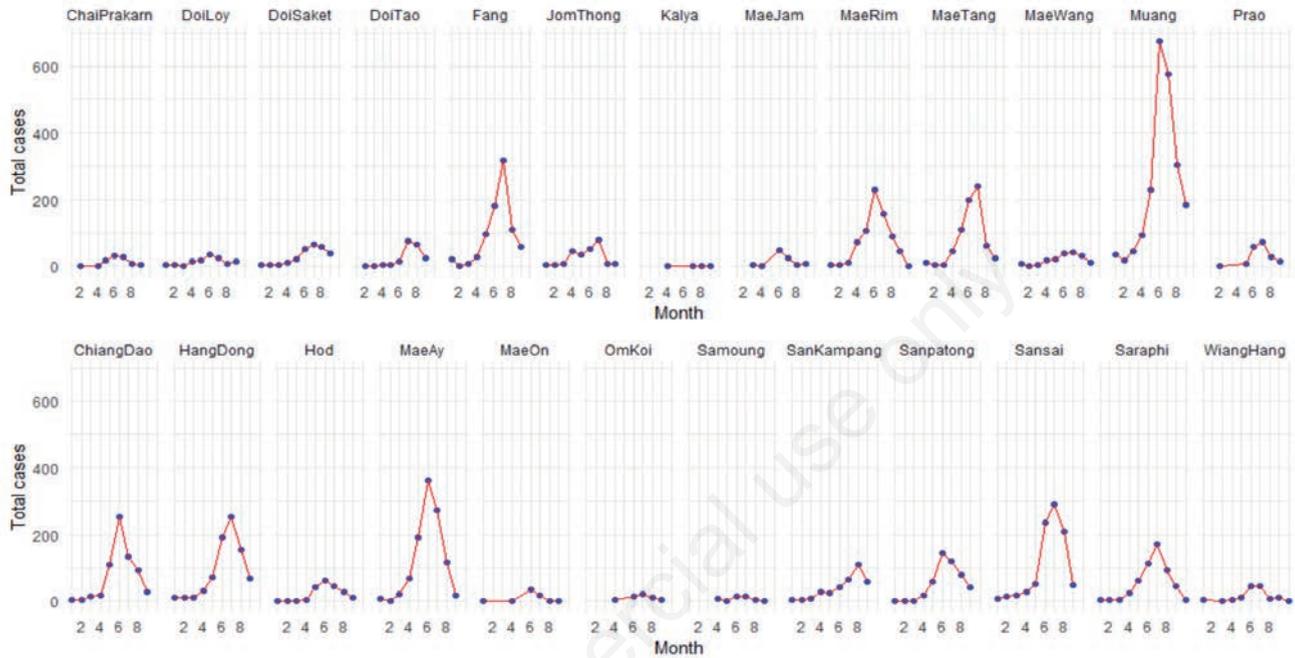
Figure 3. Number of dengue cases by month for each district in Chiang Mai in 2013.

Table 1. Space–time dengue disease clusters in the sub-district of Suthep, Chiang Mai.

| Cluster | Location | Coordinates radius | Window (from - to) | Time frame | Total | Dengue cases | | Permutation test statistic | P-value |
						Expected	Observed/ expected		
Primary									
Cluster 1	CMU	494860, 2078490	0.51	2013/7/19 2013/9/21	128	58.76	2.18	34.866	<0.0001
Secondary									
Cluster 2	Huay Keow, Paha, CMU	495126, 2080264	1.79	2013/4/26 2013/6/08	35	11.10	3.15	16.779	<0.0001
Cluster 3	Mai Lungmor, Wing41, Suan Dok	496348, 2077439	0.28	2013/6/30 2013/7/02	10	0.80	12.57	16.177	<0.0001
Cluster 4	Lingha, Mai Lungmor, CMU, Umong, Wing 41, Paha	495361, 2077587	0.79	2013/6/05 2013/6/29	65	31.28	2.08	14.809	<0.0001
Cluster 5	CMU, Paha	495995, 2078546	0.36	2013/7/06 2013/7/14	14	2.39	5.85	13.241	0.002
Cluster 6	Huay Sai, Sai Kham	494024, 2074378	0.32	2013/7/20 2013/7/30	8	0.62	12.94	13.143	0.002
Cluster 7	Pong Noi, San Lomchoy, Ram Poeng, Sai Kham	494411, 2075183	0.43	20/06/13 20/06/13	7	0.59	11.81	10.909	0.03

Cluster 1 had the highest number of cases and the longest time frame of disease occurrence. In terms of time, the first dengue cluster (Cluster 2) covered late April to early June. Cluster 3 was identified during June and July whereas Cluster 4 was found in June and Cluster 5 and Cluster 6 in July. Cluster 7 had the shortest time period with 7 cases occurring during 1 day only. CMU was the most common area for dengue occurrence and included four clusters (Clusters 1, 2, 4 and 5). Another important area was Paha Village with 3 clusters.

Discussion

This study highlights the likelihood of significant clusters for dengue in the study area and is the first study of using space-time cluster analysis for dengue in Chiang Mai at the micro-level, *i.e.* the household. The results indicate that public health agencies should communicate, campaign and create surveillance plans with a focus at the local level. Most of the space-time clusters were observed in densely populated areas (Figure 4) and produced results in agreement with a previous report which showed that local meeting points, *e.g.*, workers' hostels, have a high rate of dengue morbidity (Loshini *et al.*, 2015).
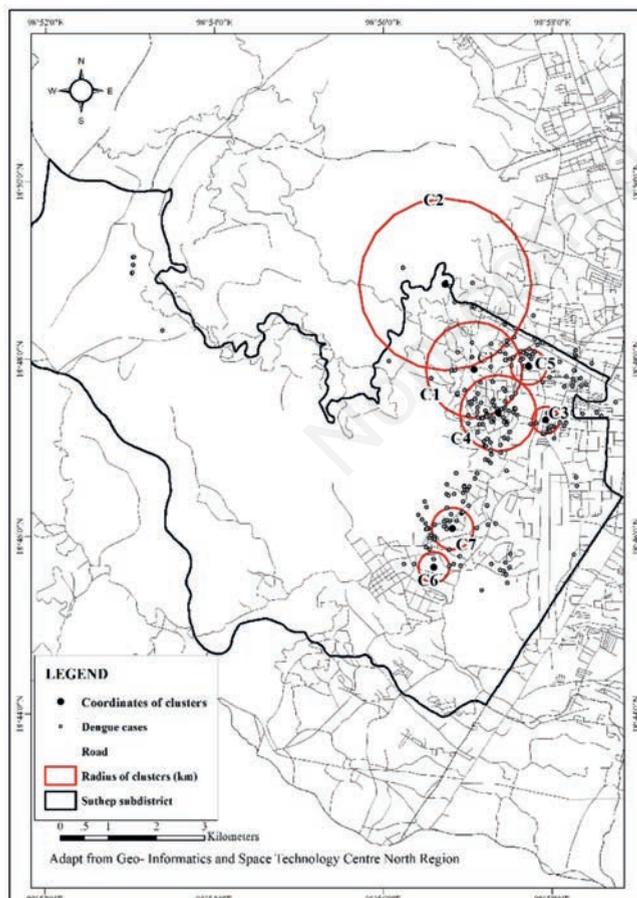
Figure 4. Space-time dengue clusters in the sub-district of Suthep in 2013.

The primary cluster was the CMU campus area which has a large student population, and Cluster 2 also encompassed a large population that represents a concentration of households, dormitories, hostels, shopping malls and night markets. Similarly, the Paha area, which presented 3 different clusters, has a high number of Buddhist monks and novices living in temples. Similar reasoning can be used to explain Clusters 4 and 5 as they covered both the CMU and the Paha area. The same pattern appeared in Clusters 4, 6 and 7, which included high density of construction labour camps. Each of the areas mentioned include a large transient population and it needs to be investigated if that could be a factor with respect to transmission. Several other questions also remain to be answered *e.g.*, why Cluster 1 stretched out over a very long period compared to the other clusters and what kind of environmental factors contributed to the disease clusters. In-depth investigation of this should be performed in the future.

Most reports in Thailand have used large spatio-temporal scales such as a province or a district. Although some recent studies in north-eastern Thailand highlight the use of sub-district data (Phanitchat *et al.*, 2019; Xu *et al.*, 2019), the lowest administrative level, no previous study has used a real fine-scale spatial dengue pattern, such as at that represented by households as done here. Surveillance at this level might well be crucial, not only for local control but also for management and prioritizing public health action nationally. The main limitation of our paper is due to a lack of geographical data from the hospital database currently in use. However, we have shown that it is indeed feasible to obtain the highest resolution data by conducting field surveys. On the other hand, this approach becomes both expensive and time-consuming when conducted on a large scale. Still, the findings presented here may help develop an understanding and awareness among people in the clusters regarding the disease outbreak.

Conclusions

This study demonstrated the process of space-time analysis for dengue outbreaks and the feasibility of such analysis, even with some limitations in terms of missing geographical data and instances of incomplete hospital data. All 6 secondary clusters in the sub-district with the highest number of infections were identified in urban areas with a high population density and most of them occurred during the rainy season (June and July). This first study using a space-time model of dengue distribution at the household level in Chiang Mai may support public health agencies to improve an effective surveillance programme disease to prevent the disease.

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