

Space-time scan statistics of 2007-2013 dengue incidence in Cimahi city, Indonesia

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Abstract

Dengue fever threatens more than 200 million people in Indonesia. The disease has spread to over 400 of Indonesia's 497 districts, 26 of which have been declared hyper-endemic. These districts are all situated in West Java, the most densely populated province in the country. A study was conducted to detect clusters of dengue incidence during 2007-2013 in Cimahi City, which is situated in the Bandung metropolitan area in West Java. A temporal-spatial analysis based on population data from the local Bureau of Statistics, and monthly analysis of dengue incidence from the local Municipality Health Office, were performed using SaTScan™. This retrospective space-time analysis with

a Poisson distribution model and monthly precision revealed 24 significant clusters ($P < 0.001$) throughout the seven-year study period. The most likely cluster was detected in the centre of Cimahi City and followed as it moved to the northern part of the city. Several primary and secondary clusters were identified in villages surrounding Cimahi City over time, and our conclusion is that we identified a dynamic spread of dengue fever initiated from the city centre to surrounding areas during the study period. In general, clusters were more common in the first quarter of each year. An in-depth investigation to understand relevant risk factors in high-risk areas in Cimahi city is encouraged.

Introduction

Dengue fever (DF) is an arboviral, vector (*Aedes* mosquitoes)-borne disease that exists in four serotypes (DEN 1-4), which threatens more than 2.5 billion of the world's population. Globally, DF has increased to more than 30 times in last 50 years, resulting in more than 50-100 million infections annually (WHO, 2011; Bhatt *et al.*, 2013). It is known that the dengue virus spreads rapidly due to a high adaptive tendency of the *Aedes* species, climate change, common areas suitable as breeding sites, strong population mobility and international trade (McMichael *et al.*, 2006; Benedict *et al.*, 2007; Aranuchalam *et al.*, 2010; Gubler, 2011; Schmidt *et al.*, 2011; Bouzid *et al.*, 2014). Knowledge on epidemiological trends of the dengue virus, both spatially and temporally, in the hyper-endemics is needed to strengthen current control and prevention (Attaway *et al.*, 2014). This is particularly important as there is currently no chemotherapy or vaccines available, even if a potentially useful vaccine comes on the market in the next five years (Lang, 2009).

The first DF outbreak Indonesia was reported in Surabaya in 1968 (Sumarmo, 1987). The four circulating DEN serotypes have resulted in outbreaks in 412 of Indonesia's 497 districts. All DEN serotypes have been documented in West Java with the DEN-3 type being the predominant one (Prasetyowati and Santya, 2012). In 2013, the Ministry of Health of Indonesia (MoHI) reported 112,511 cases (DF incidence rate of 41.25 per 100,000 population) and 871 deaths corresponding to a case fatality rate of 0.7% (Ministry of Health of Indonesia, 2014). Almost 20% of the total population live in West Java, which makes it one of the most densely populated province in the country. West Java has 26 districts declared as hyper-endemic (2013 incidence rate: 50.55 per 100,000 people; case fatality rate: 0.7%). Cimahi City had the highest DF incidence rate in West Java in 2013. For the last ten years, more than 12,000 DF incidence and 84 deaths was reported in the city (Cimahi Municipal Health Office, 2014). Cimahi City is part of the Bandung metropolitan area, which is an endemic region and in the fourth most densely populated city (Porter *et al.*, 2005). Incipient

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insecticide resistance and relevant studies on epidemiological situation regarding the DF spatial-temporal distribution in Indonesia, specifically in Cimahi City, control and prevention remain inadequate (Astuti *et al.*, 2014).

In order to enhance our understanding about distribution and DF trends over time, we performed a retrospective spatial-temporal analysis on DF incidence over 2007-2013 in Cimahi City. However, to our knowledge, this is the first study on spatial-temporal analysis using space-time scan statistics to investigate the DF trend in West Java. This approach for various health-related matters has been documented, both for infectious diseases (DF, malaria, tuberculosis) and non-communicable diseases epidemiology (*i.e.* cancer) (Kulldorff *et al.*, 1998; Morrison *et al.*, 1998; Touray *et al.*, 2010; Jeefoo *et al.*, 2010; Schmidt *et al.*, 2011; Wu *et al.*, 2011; Bi *et al.*, 2013). Surveillance and early detection should be prioritized in the face of the global DF threat (Guzman *et al.*, 2010). Thus, identification of the distribution pattern of DF cases is required to discover the spread of the disease in Cimahi City. Our study aimed to investigate: i) the presence of high-risk DF clusters in this area; and ii) the temporal distribution pattern of detected such cluster over the seven-year period.

Materials and Methods

Study site

With more than 43 million people at an average density of 1222 people per km², West Java has the highest population in Indonesia (Bureau of Statistics of Indonesia, 2014). Cimahi City comprises three sub-districts or *Kecamatan* (North Cimahi, Centre Cimahi, and South Cimahi) and fifteen villages known as *Kelurahan* (Cibabat, Cipageran, Citeureup, Pasirkaliki, Baros, Cigugur Tengah, Cimahi, Karangmekar, Padasuka, Setiamanah, Cibeber, Cibeureum, Leuwigajah, Melong, dan Utama). It should be noted that Cimahi is also the name of a village belonging to the larger entity of Cimahi City. The population density varies in each *Kelurahan*, from 79.01 to 236.10 people per km². The city is located around latitude 6°53'S and longitude 107°32'E (Figure 1), covers an area of 40.37 km² and has a total population of 561,368 people (Cimahi Municipal Bureau of Statistics, 2014).

Data

For the purpose of analysis, we obtained a 7-year period of hospital-confirmed DF incidence data (2007-2013) from the Cimahi Municipal Health Office. Village-level population data were obtained from the Cimahi Municipal Bureau of Statistics (Cimahi Municipal Bureau of Statistics, 2014). For spatial geo-reference needs, 15 village coordinates (latitude/longitude) were obtained by geo-coding each village offices (*Kantor Kelurahan*) to represent each geographical location on a Google Maps application.

Spatial-temporal analysis

We downloaded the free, space-time statistics software SaTScan™ ver.9.4 (SaTScan, 2015) that was originally developed by Martin Kulldorff (Kulldorff and Nagarwalla, 1995). Applications of this software has been used for various purposes and accordingly documented (Kulldorff *et al.*, 1998; Schmidt *et al.*, 2011; Bi *et al.*, 2013; SaTScan, 2015). In our study, we used retrospective space-time analysis with a Poisson model to identify villages at high risk for DF during between 1 January 2007 and 31 December 2013. By default, the maximum spatial

cluster size is set at 50% of the population at risk to reduce bias (Kulldorff and Nagarwalla, 1995). However, our study used a modified maximum spatial cluster size of 15% of the total population at risk to avoid overlapping. This was felt to be acceptable considering the high population density and the size of the area selected for study. A circular window shape was chosen and the size of maximum temporal cluster set at 50% of the total population at risk to detect possible sub-clusters. No space-time trend adjustments were performed. A Monte-Carlo approach with 9999 repetitions was performed to test null hypothesis that there was not difference of relative risk (RR) between DF clusters. P values <0.0001 were considered as statistically significant. The cluster with the highest log-likelihood ratio (LLR) was determined as the most likely cluster, while the others with lower LLR defined as secondary clusters (SaTScan, 2015). To visualise the cluster pattern in a geographical context, the geographic information system (GIS) software ArcGIS, version 9.0 (ESRI Inc., Redlands, CA, USA) were used.

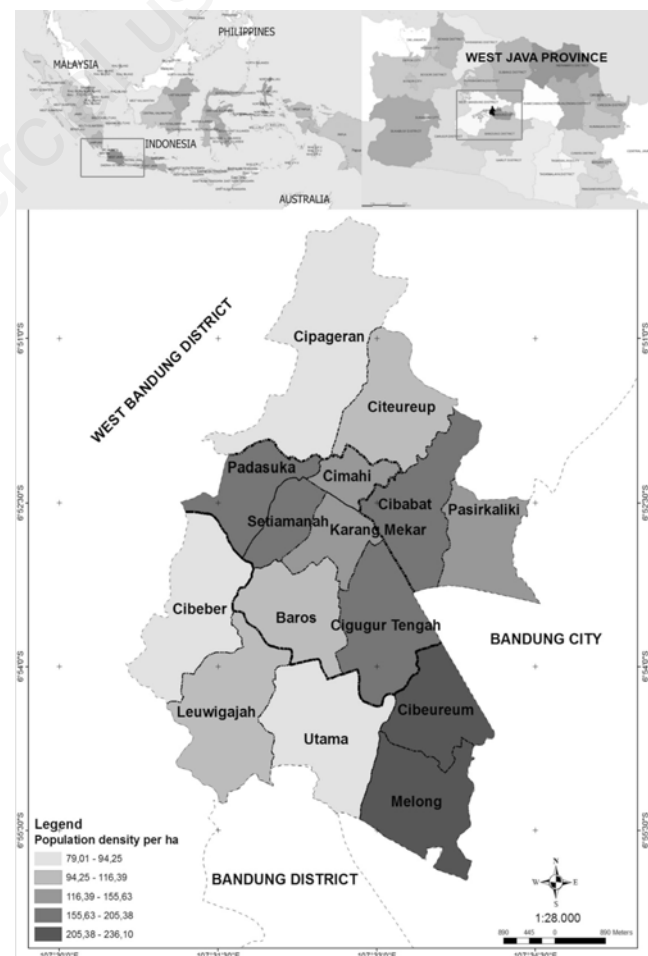


Figure 1. Geographical location of Cimahi City and its surrounding 15 villages.

Results

Based on a monthly DF data from the seven-year study period, our space-time analysis detected a total of 24 clusters (Table 1). These DF clusters were initially spatially concentrated in the centre of Cimahi City but moved towards the northern region by the end of the study.

At the first quarter of 2007, we identified seven significant clusters ($P < 0.001$). A most likely cluster, with RR of 2.16 covered the three villages Cibabat, Cimahi, and Karangmekar ($P < 0.001$; 12% of the total population), was discovered. There were six secondary clusters, one of which (Cibeber) had more than three-fold RR than the other clusters. In the second year of study, a most likely cluster, covering Cibabat and Cimahi (RR=2.53; $P < 0.001$) with more than 50,000 population at risk was detected. However, there were only three secondary clusters this year and they covered the four villages of Cipageran, Citeureup, Baros and Cibeureum. In January-April of 2009, Cibabat and Cimahi along with Padasuka formed a most likely cluster (RR=2.98; 7% of the total population).

In the first two-months of 2010, a most likely cluster was observed in the three villages of Cimahi, Karangmekar and Setiamanah (RR=2.96; $P < 0.001$; 61,041 population at risk). The villages Baros, Cipageran and Citeureup were secondary clusters. At the fifth-year of study period, only two clusters were identified, but with greater risk (RR > 3.8). They occurred from January-September, d included Citeureup and Cimahi. In February 2012, Citeureup again showed a cluster, but this time with higher relative risk (RR=5.77; $P < 0.001$). Furthermore, in the first half of 2013 Cipageran was covered by a cluster (RR=2.80; $P < 0.001$). In addition, Cimahi was also identified as a secondary cluster in both mid-

2012 and mid-2013 with a high relative risk documented in 2013 (RR=4.55; $P < 0.001$; 14,879 population at risk). All clusters found are depicted in Figure 2.

Discussion

Statistically significant high-risk DF clusters with various RR were discovered in almost all villages in the Cimahi City in the seven-year period 2007-2013 and a retrospective space-time analysis detected 24 additional significant clusters ($P < 0.001$). A dynamic distribution of most likely clusters was seen to spread from the centre of Cimahi City northwards. We found that two of the villages, Cibabat and Cimahi, were most frequently detected as covered by most likely clusters, specifically during the first four years of the study. Citeureup emerged as a most likely cluster in 2011-2013. Temporally, most likely clusters were observed in the first quarter of the year. Most most-likely-cluster geographically centred on a high-populated area with crowded housing situated adjacent to the provincial main road connecting Cimahi City with its neighbours, West Bandung District and Bandung City. Our findings show an evidence of a significant spatio-temporal distribution of DF high-risk areas in the study area.

Although there is still limited use of applied spatio-temporal techniques to understand DF epidemiology in Indonesia, some studies had started to apply GIS approaches. For example, Astutik *et al.* (2011) used Moran's autocorrelation for DF study in East Java, whereas others have used descriptive GIS and/or remote sensing techniques to document DF in some endemic districts in West Java, such as Ciamis and Banjar

Table 1. Space-time cluster analysis with monthly precision of dengue incidence for Cimahi City 2007-2013.

Year	Cluster type	Area (village level)	Period	Radius (km)	Actual cases (n)	Expected cases (n)	People at risk (n)	RR	LLR	P
2007	Most likely	Cibabat, Cimahi, Karangmekar	1/1/2007-30/4/2007	1.44	224	109	71,048	2.16	49.31	<0.001
	1 st secondary	Padasuka, Setiamanah	1/1/2007-28/2/2007	1.41	122	46.16	61,203	2.73	43.97	<0.001
	2 nd secondary	Cibeber	1/1/2007-28/2/2007	0	54	15.07	19,984	3.64	30.30	<0.001
	3 rd secondary	Cigugur Tengah	1/2/2007-31/7/2007	0	203	114.57	49,514	1.84	29.43	<0.001
	4 th secondary	Cipageran	1/1/2007-28/2/2007	0	76	28.01	37,129	2.77	28.37	<0.001
	5 th secondary	Cibeureum	1/2/2007-28/2/2007	0	59	22.09	61,709	2.71	21.34	<0.001
	6 th secondary	Utama	1/1/2007-28/2/2007	0	67	27.55	36,527	2.47	20.42	<0.001
2008	Most likely	Cibabat, Cimahi	1/1/2008-30/4/2008	1.09	106	44.08	53,411	2.53	32.68	<0.001
	1 st secondary	Cipageran, Citeureup	1/1/2008-31/3/2008	0.74	94	41.96	67,608	2.34	24.89	<0.001
	2 nd secondary	Baros	1/1/2008-31/5/2008	0	58	23.99	23,144	2.49	17.65	<0.001
	3 rd secondary	Cibeureum	1/1/2008-29/2/2008	0	36	12.20	61,709	3.01	15.37	<0.001
2009	Most likely	Padasuka,	1/1/2009-30/4/2009	0	140	49.25	41,600	2.98	57.61	<0.001
	1 st secondary	Cibabat, Cimahi, Karangmekar	1/1/2009-30/6/2009	1.44	255	136.5	76,440	1.99	44.62	<0.001
	2 nd secondary	Citeureup	1/1/2009-30/4/2009	0	112	45.4	38,360	2.55	35.63	<0.001
2010	Most likely	Cimahi, Karangmekar, Setiamanah	1/1/2010-28/2/2010	0.73	85	29.61	61,041	2.96	35.11	<0.001
	1 st secondary	Baros	1/1/2010-31/5/2010	0	74	32.04	25,806	2.37	20.48	<0.001
	2 nd secondary	Cipageran, Citeureup	1/1/2010-31/3/2010	0.74	102	58.66	79,267	1.78	13.63	<0.001
2011	Most likely	Citeureup	1/1/2011-30/6/2011	0	49	13.92	35,182	3.81	27.94	<0.001
	Secondary	Cimahi	1/5/2011-30/9/2011	0	24	4.67	13,950	5.36	20.37	<0.001
2012	Most likely	Citeureup	1/2/2012-29/2/2012	0	24	4.25	36,508	5.77	21.99	<0.001
	1 st secondary	Cigugur Tengah	1/6/2012-30/6/2012	0	25	6.64	55,071	3.85	14.97	<0.001
	2 nd secondary	Karangmekar, Setiamanah	1/1/2012-29/2/2012	0.53	32	11.40	47,302	2.87	12.66	<0.001
	3 rd secondary	Cibabat, Cimahi	1/6/2012-31/8/2012	1.09	55	26.05	70,474	2.18	12.63	<0.001
2013	Most likely	Cipageran, Citeureup	1/1/2013-30/6/2013	0.74	129	51.34	82,438	2.80	45.38	<0.001
	Secondary	Cimahi	1/8/2013-31/10/2013	0	21	4.71	14,879	4.55	15.27	<0.001

RR, relative risk; LLR, log likelihood ratio.



(Ruliansyah *et al.*, 2011, 2014). A Standard Deviational Ellipse (SDE) model was used in Banjar City (Rahmaniati *et al.*, 2014). In contrast, there were numerous studies in mainland Asia applying space-time scan statistics to strengthen DF surveillance system in Malaysia (Cheong *et al.*, 2014), Saudi Arabia (Alzahrani *et al.*, 2013), Thailand (Jeefoo *et al.*, 2010), Bangladesh (Banu *et al.*, 2012), China (Li *et al.*, 2012), and Vietnam (Toan *et al.*, 2013).

Cimahi village, located in the heart of Cimahi City (Figure 1) with 15,563 persons per km² next to Karangmekar and Cibabat (Cimahi Municipal Bureau of Statistics, 2014), was consistently identified as a most likely cluster between 2007 and 2010 and appeared as a secondary cluster in 2011-2013. These three villages have identical landscape characteristics with dense settlement adjacent to the main road. As an obvious clustered pattern, we found that the high-risk areas spread significantly from the centre to north during the timeframe of the study. A plausible explanation for this phenomenon was that the potential transmission might have occurred in the centre of the city, where most people interacted strongly with each other in schools, offices and market places regardless of having very different health status backgrounds. Occurrence of potential breeding sites in public spaces, vector populations and highly mobile people (commuters) facilitated the spread of DF (Weiss and McMichael, 2004; Wearing and Rohani, 2006). Similar trend has been documented in Thailand, where DF evidently expanded to non-endemic areas (Strickman *et al.*, 2000). Hence, further investigation is needed to identify potential risk factors in these high-risk clusters.

The dynamic spread of high-risk areas within Cimahi City during the seven-year study indicates that there was interrelated association between vector, host, and the environment. For example, many different associations of DF outbreaks with various climate and socio-economic variables have been reported (Johansson *et al.*, 2009; Banu *et al.*, 2011; Åström *et al.*, 2012; Oki and Yamamoto, 2012; Ariati and Musadad, 2013; Naish *et al.*, 2014; Ariati and Anwar, 2014; Bouzid *et al.*, 2014; Dhimal *et al.*, 2015). A study on knowledge, attitude, and practices in Cimahi was performed by Pradani *et al.* (2010), who concluded that people often show inconsistent preventive measure practices in spite of good perception and knowledge of DF risk factors. A study on vector resistance found that the insecticide *cypermethrin* was no longer effective when used to control *Aedes aegypti* populations in Cimahi City (Astuti *et al.*, 2014). There are some evidence of DF incidence being associated with seasonal variation, where higher DF incidence commonly occurred at the end of the rainy season (March-April). Concurrent findings come from Ariati *et al.* (2014), who developed a climate-based prediction model for hemorrhagic DF in Bogor city. In our study, it was clear that most clusters occurred in the first quarter of the year.

This report should be seen as pilot study as our results do not estimate RR precisely due to lack of information on some influential aspects, *i.e.* vector density and related environmental and socioeconomic characteristics, *e.g.* age, gender, immunity, land-use, and climate. We also suggest that some analytical adjustments need to be considered in future works to obtain more comprehensive information as

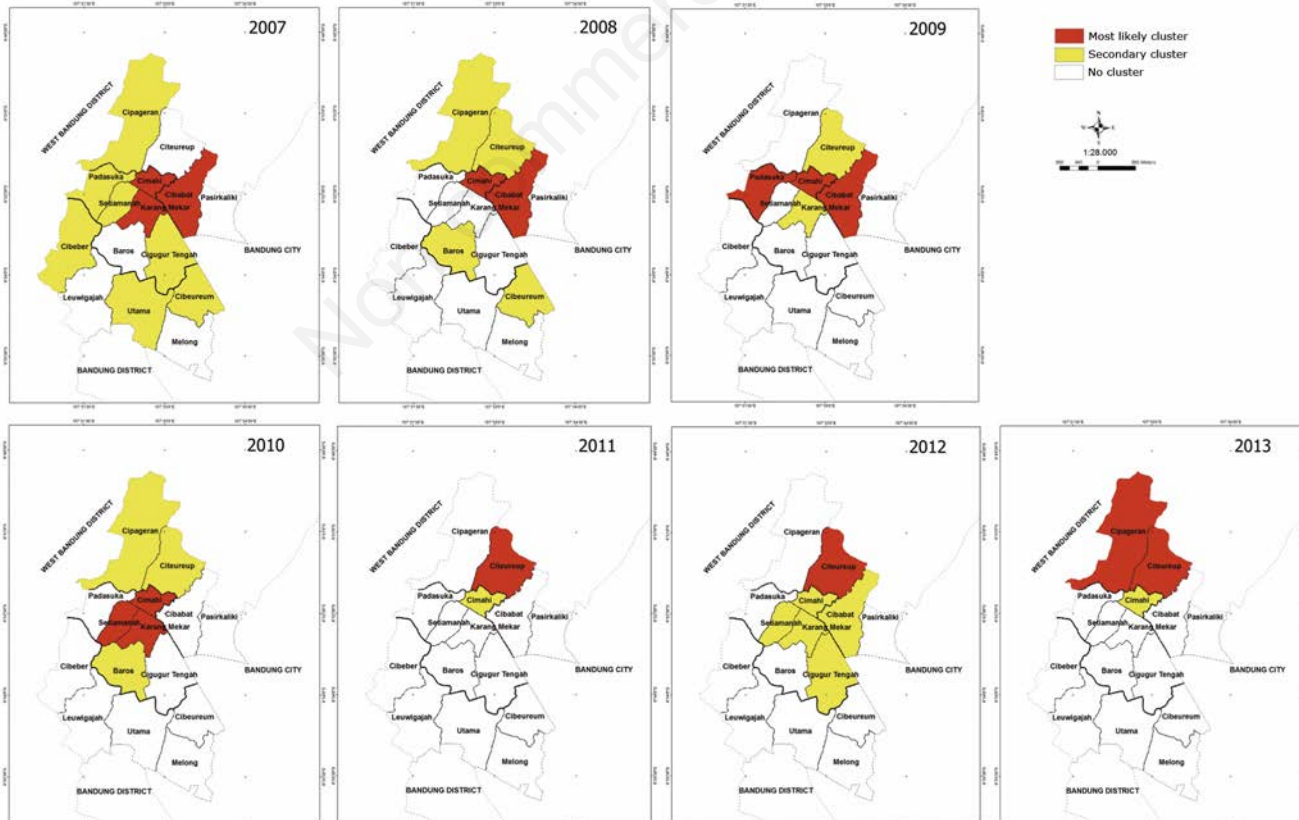


Figure 2. Clusters of dengue fever found during the period covered by the study.

pointed out by Naish *et al.* (2014). However, our study has produced a perspective on DF incidence in an endemic region in Indonesia that can be used by local health managers and disease surveillance staff to monitor DF outbreaks and facilitate decisions on how to mount an effective intervention. This information would also be beneficial for communities by encouraging people's awareness with respect to their environment and preparedness to deal with DF outbreaks based on temporal trends. Another strong point is that we used the village-level as the smallest unit of analysis, which makes it possible to estimate inter-cluster RR risk in the area. The results presented thus have several implications for the current surveillance system and we recommend that: i) more active surveillance be routinely applied to monitor every change on DF epidemiology over time as suggested by WHO (2011); ii) GIS applications be used as operational supportive tools for projection and intervention with regard to areas at high risk for DF; iii) future studies to explore the major inter-related factors in a larger areas be considered to study outbreaks, which may have resulted from high migration over the districts; iv) our health system be strengthened in context of disease control and prevention by the creation of inter-sectoral partnerships involving health, education, environment and general affairs to provide better coordination with regard to infrastructure, housing and demography resulting in a big picture of DF distribution pattern and allowing in-depth analysis.

Conclusions

Twenty-four statistically significant DF clusters were identified in the 2007-2013 period. Clusters were most frequently detected as in the first 4-year period of study in the villages Cibabat and Cimahi, whereas Citeureup emerged as a high-risk cluster in 2011-2013. Importantly, DF clustering was more often observed in the first quarter of each year and there should be a tendency of spread from the centre to the northern part of Cimahi City. Future research on risk factors is strongly recommended.

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