Tropical Biomedicine 32(4): 587–597 (2015)

Evaluation of land cover and prevalence of dengue in Malaysia

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Received 12 October 2014; received in revised form 4 February 2015; accepted 19 April 2015

Abstract. Serological confirmation of dengue in 1,410 school-going children aged 7-18 years provided prevalence data for 16 different sites in Malaysia. These sites ranged from highly urbanized cities to small towns. We found that at least ~7 % of children in the study group had been exposed to dengue by age 12 and ~16% by age 18. Here we report that the dengue seroprevalence correlates with i) increasing land development and decreased vegetation, and ii) the overall population growth. Water bodies did not significantly affect dengue prevalence. High prevalence of dengue was also recorded in few of the non-urban sites suggesting the expanding geographical locality of those who get dengue in Malaysia in tandem with increased land usage activities. These findings highlight the need to give closer consideration to future urban planning and development, taking into consideration the changing demography and the importance of built environment to mitigate the increasing incidence of dengue in the non-urban areas of Malaysia.

INTRODUCTION

Dengue is a mosquito-borne disease present in over 125 countries globally. More than 2.5 billion people living in the tropics and sub-tropics are at risk of contracting the infection with almost 50 million new infections reported annually (World Health Organization, 2009; Azil *et al.*, 2011). The disease is transmitted to humans by its vectors, *Aedes aegypti* and *Aedes albopictus*, which are generally present in urban and sub-urban areas, respectively. The steady rise in dengue cases through the years, as much as 30-fold over the past 50 years (World Health Organization, 2002), as well as its geographic expansion to other non-traditional dengue endemic regions have been attributed to many factors including climate change, urbanization and rapid population growth and population movement (Gubler, 2002).

Dengue is hyperendemic in Malaysia where all four dengue virus serotypes co-circulate and cause regular recurring outbreaks (AbuBakar & Shafee, 2002). The number of dengue cases has increased as much as four folds over the past decades, from ~44 cases/100,000 population in 1999 to ~181 cases/100,000 population in 2007 (Ministry of Health Malaysia, 2008). Also, from 1999 to 2007, the incidence rate for dengue was constantly much higher in those more than 15 years of age. Over fifty percent of all dengue cases in Malaysia are currently recorded from two major states, Selangor and Kuala Lumpur, the two most developed and populous states (Ministry of Health Malaysia, 2008). However, increasing numbers of dengue cases are also being reported in other less developed states including Kelantan, Pahang and Negeri Sembilan (Hussin *et al.*, 2005; Ahmad Nizal *et al*., 2012; Mohd-Zaki *et al*., 2014).

There are a number of studies that have related land use and land cover to dengue transmission and incidence. Changes to land use was found to affect dengue and vector population (Vanwambeke *et al*., 2007) while land built-up area had the highest impact on the incidence of dengue (Nakhapakorn & Tripathi, 2005). Areas with low vegetation (Nazri *et al*., 2011; Araujo *et al*., 2014; Cheong *et al*., 2014) and the presence of water bodies and wetlands favored dengue infection (Cheong *et al*., 2014; Sheela *et al*., 2014). In Malaysia, studies on land cover features and dengue prevalence have been carried out in a small number of states. Studies describing land cover features and dengue have only so far been conducted in Selangor (Din *et al*., 2007; Umor *et al*., 2007, Cheong *et al*., 2014). Hussin *et al*. (2005) described dengue fever in the state of Kelantan although they did not evaluate the relationship between surrounding land cover and dengue. Nazri *et al*. (2013) and Er *et al*. (2010) reported the clustering of dengue cases when looking at the spatial distribution of dengue cases in districts in Penang and Selangor, respectively, although surrounding environmental aspects were not discussed.

In our study, we looked at the relationship between local dengue prevalence and the surrounding land cover in different districts in Malaysia. Our study sites were located in various surroundings including highly urbanized cities and small towns. We determined the dengue prevalence in school-going children at each site and then delineated the surrounding land cover types, namely the extent of developed area, vegetation and water body, to evaluate their role as possible contributors to the disease. At the same time, we also looked at the age distribution of dengue seroposivity in children.

MATERIALS AND METHODS

Seroprevalance data

The samples analysed in this study were obtained from the University of Malaya's sample repository. The sera were previously anonymously collected from school children by convenience sampling. In total, we only obtained access to blood samples from 2008 – 2009 from 1,410 children aged 7 to 18 years, who were from 26 schools in Malaysia. The study protocol received ethic clearance MEC Ref No. 806.23 and 806.24 from the University of Malaya Medical Centre Ethics Committee. School children are a good population to examine as they are less likely to have travelled outside their home state as compared to the adult population and thus would better reflect the dengue prevalence in the respective local communities. Dengue IgG capture ELISA (Standard Diagnostics, Korea, Cat. no. 11EK10) was used to test for the presence of anti-dengue specific antibodies according to the manufacturer's instructions. Positive results meant a previous exposure to dengue virus, either from a recent or past infection.

Study sites

The 26 school sites were located using Google Earth™ based on their registered addresses (Table 1). At the time of analysis, images in Google Earth™ were dated 2007 - 2009. These schools were conveniently selected from the list of available sites to include communities situated in highly populated and urbanized locations to areas with much lower population and modest infrastructure. In five of the sites where the exact location of the school could not be pinpointed, either due to the presence of clouds (JHR1, SEL1, PAH1 and KEL1) covering the area and to poor image resolution (JHR1 and PER3), the road on which the school is located was taken as the location of the school site. In six of the sites (JHR1, JHR2, KL1, PER1, PER3 and KEL1), data from two or three schools within close proximity to each other were grouped together as a site resulting in 16 study sites. These sites were located in nine Malaysian states mostly along the west coast of Peninsular Malaysia: Federal Territory of Kuala Lumpur (KL1, n=177), Selangor (SEL1, n=21), Perak (PER1, n=57; PER2, n=21; PER3, n=131;), Kedah (KED1, n=20; KED2, n=111), Penang (PEN1, n=44; PEN2, n=69),

Table 1. Tabulation of seropositivity, proportion of land cover, and population density data for the study sites. Sites were also grouped depending on the percentage of developed land: highly developed (> 30%), moderately developed (>20%) and least developed (<20%)

	Study site	Latitude	Longitude	District	State	Seropositivity for dengue-specific IgG (%)	Land cover types			Population density (District level)* ('000)
							Development (%)	Water body (%)	Vegetation (%)	
Highly developed (Urbanized)	KL1	3°11'6.16"N	101°39'11.07"E	WPKL	Kuala Lumpur	24 (*n*=43/177)	78	2	20	6705
	JHR3	1°31'55.36"N	103°48'6.44"E	Johor Bharu	Johor	11 (*n*=6/55)	51	9	40	784
	PEN1	5°20'33.04"N	100°28'31.99"E	S.P. Selatan	Penang	9 (*n*=4/44)	43	10	48	639
	PER3	4°49'31.18"N	100°42'30.58"E	Larut&Matang	Perak	8 (*n*=11/131)	40	3	57	151
	KEL1	6°8'14.65"N	102°14'18.30"E	Kota Bharu	Kelantan	26 (*n*=15/58)	35	10	56	1204
	SBH1	5°59'14.09"N	116°5'59.34"E	Kota Kinabalu	Sabah	6 (*n*=12/191)	30	35	31	1274
	PEN2	5°23'46.09"N	100°22'4.75"E	S.P. Tengah	Penang	9 (*n*=6/69)	30	44	26	1577
	KED1	5°21'47.88"N	100°33'16.30"E	Kulim	Kedah	0 (*n*=0/20)	30	2	68	324
Less developed	KED2	5°25'38.80"N	100°31'54.10"E	Kulim	Kedah	7 (*n*=8/111)	29	2	69	324
	PER1	4°33'53.06"N	101°2'50.14"E	Kinta	Perak	12 (*n*=7/57)	26	14	60	421
	PAH1	3°47'6.11"N	103°17'21.58"E	Kuantan	Pahang	16 (*n*=28/176)	26	16	58	140
	SEL1	3°0'15.20"N	101°24'47.83"E	Klang	Selangor	10 (*n*=2/21)	26	16	58	1297
	PER2	4°49'26.09"N	101°5'23.21"E	Kuala Kangsar	Perak	5 (*n*=1/21)	21	4	74	65
Least developed	JHR2	1°39'4.41"N	103°36'14.47"E	Johor Bharu	Johor	4 (*n*=5/128)	14	0	86	784
	JHR1	1°29'21.96"N	103°23'18.89"E	Pontian	Johor	6 (*n*=8/125)	4	44	53	189
	KEL2	6°2'38.70"N	102°8'44.56"E	Pasir Mas	Kelantan	0 (*n*=0/26)	1	4	95	352

* Based on 2008 data obtained from the Department of Statistics Malaysia.

and Johor (JHR1, n=125; JHR2, n=128; JHR3, n=55) to the south. Two sites were located in the east coast of the Peninsular: Pahang (PAH1, n=176) and Kelantan (KEL1, n=58; KEL2, n=26). One site was in Sabah (SBH1, n=191) in East Malaysia.

At each study site, the land cover types (developed land, vegetation and water bodies) were assessed within an area of a 10 km radius, since public schools in Malaysia generally only admit students living within a 10 km radius of a school. Developed land was defined as all residential, commercial and industrial areas where human presence is constant and usually permanent. Vegetation included natural forests, plantations and agricultural land. Water bodies included lakes, wetlands, rivers and seas. Visual estimation of the proportion of land cover types was calculated from the Google Earth images. To aid in the calculation, the image was overlaid with a grid generated by GE-Path 1.4.4. Each grid cell had an area of 1 km^2. At each study site, the number of grid cells that were designated as developed land, vegetation and water bodies were enumerated. Each land cover variable was then presented as the percentage of the total area. Cloud cover was present in some sites but was generally sparse and did not obstruct the identification of land cover type. The population density for 2008 of the respective district was available from the Department of Statistics Malaysia (http://www.statistics.gov.my, Accessed 28 December 2009). The sites were then arbitrarily categorised into highly developed, moderately developed and least developed depending on the amount of developed area within each study area (Table 1). The country's population data from the years 1973-2008 were obtained from the Department of Statistics, Malaysia. The number of dengue cases for the same period was obtained from the Ministry of Health Malaysia. The data was then analysed to look for correlation between the two variables.

Spearman's rank-order correlation was used to assess the relationship between dengue prevalence and the land cover variables and population data. The analyses were performed using GraphPad Prism v5.02 (GraphPad Software Inc., USA).

RESULTS

The locations of all sixteen study sites as well as the local dengue prevalence are illustrated in Figure 1. Of the total 1,410 samples, 156 (~11%) samples were positive for dengue-specific IgG antibodies. At individual sites, seropositivity ranged from 0% to 25±1% (Table 1). Amongst the four age groups, the 16-18 years showed the highest sero-prevalence (Figure 2), followed by the 13-15, 7-9 and 10-12 years, suggesting cumulative exposure to dengue over time.

The possible relationships between dengue seroprevalence and the various land cover features are shown in Figure 3. The sites examined were mostly located in residential areas. For schools located in large cities, such as Kuala Lumpur, Johor Baru and Penang, residential areas consisted of interconnected or linked houses laid out closely. The area of highly developed land occupied more than a third of the study area and vegetation was scarcely visible from the satellite imagery. Residential areas in moderately developed towns consisted of interconnected houses that were usually interspersed with construction areas as observed for sites in Perak, Johor and Kedah. In Kelantan, interconnected houses and single traditional wooden houses were common and visible patches of vegetation were interspersed amongst the houses. Sites in the least developed area had largely agricultural lands and houses were interspersed.

The seroprevalence of dengue in the community was defined arbitrarily in this study as low (<5%), intermediate (5-10%) and high (>10%). It was found to be significantly linked with the extent of developed land (r_s=0.54, 95% CI = 0.04 to 0.82, $p<0.05$) and vegetation (r_s=-0.54, 95% CI = -0.82 to -0.05, $p<0.05$) at each site. Overall, high sero-positivity was observed in sites with high developed land and low vegetation.

Large water bodies did not appear to influence dengue prevalence (r_s=0.26, 95% CI = -0.29 to 0.68, $p>0.05$). Sites where water bodies occupied much of the total area were largely attributed to rivers (PAH1, KEL1, KEL2 were situated next to the river), seas

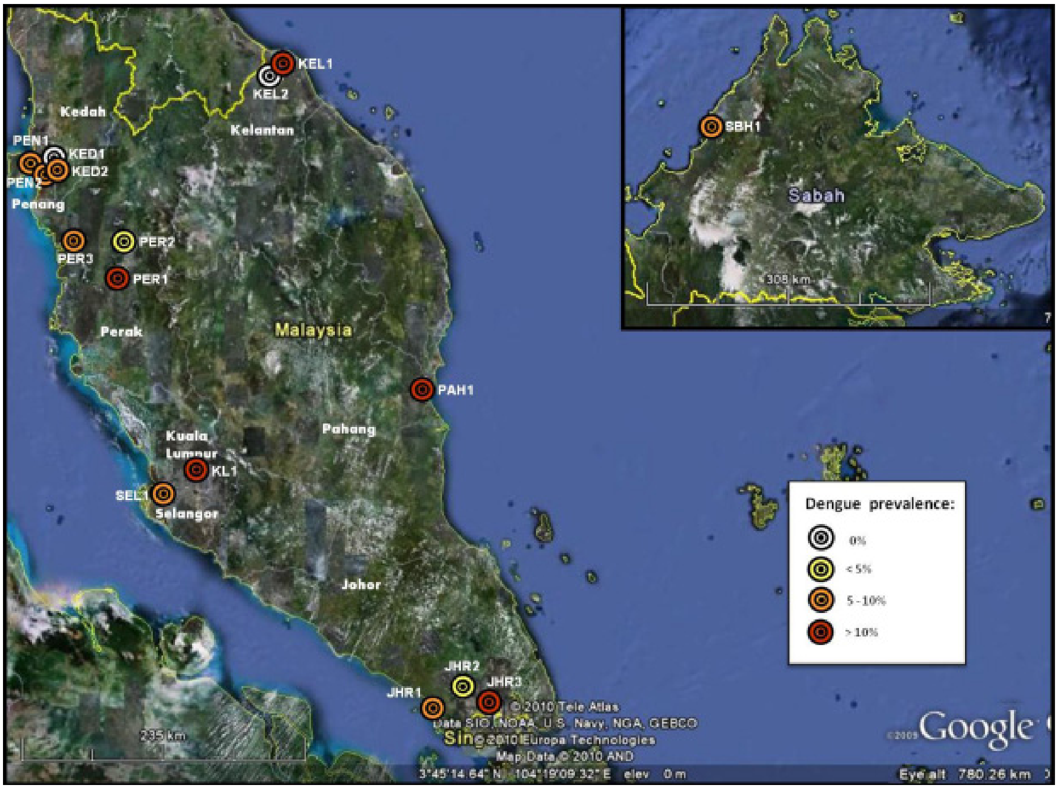

Figure 1. Seroprevalence of dengue at the different study sites in Malaysia.
The percentage of dengue prevalence at each site is presented as differently coloured concentric circles with red circles being the highest. The map was extracted from Google Earth™.

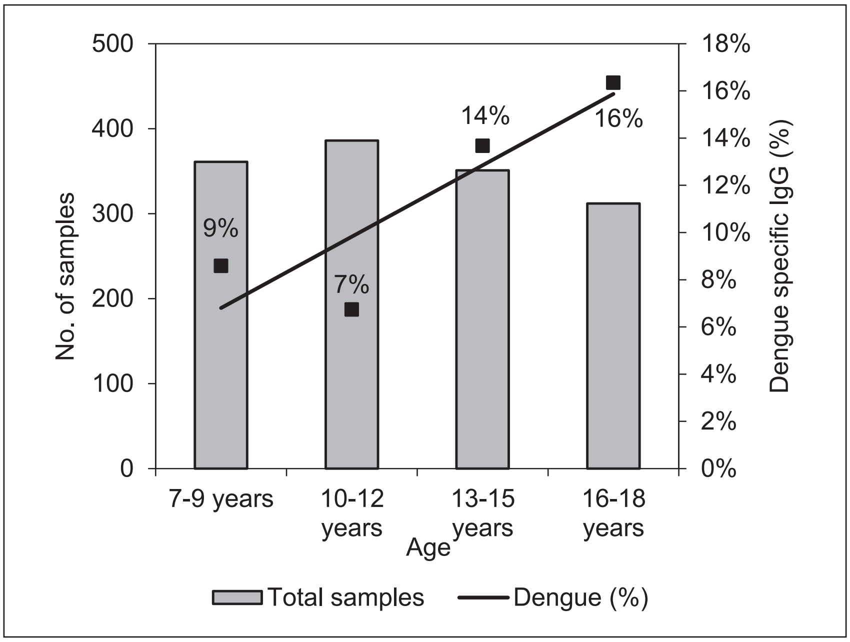

Figure 2. Dengue seroprevalence of the study population by age groups.

(PAH1, JHR1, PEN2, KEL1, SBH1, SEL1 were in coastal towns) and abandoned tin mine pools (PER1, PER2). For sites situated near rivers and coasts, only PAH1 and KEL1 had high seroprevalence (>10%), however the water bodies only accounted for 16% and 10% of the total study site area, respectively. For sites near mining pools, PER1 had higher seroprevalence and area of water bodies compared to PER2.

In our data set, no correlation was seen between dengue and population density (r_s=0.35, 95% CI=-0.19 to 0.72, p=0.18). However, when the national data for population growth and dengue was compared, there was a significant positive correlation (r=0.89, P<0.01) as illustrated in Figure 4. It was also noted that while the number of dengue cases may fluctuate between years, the trend remained to be that of an exponential growth. This growth was observed similarly for Malaysia's population.

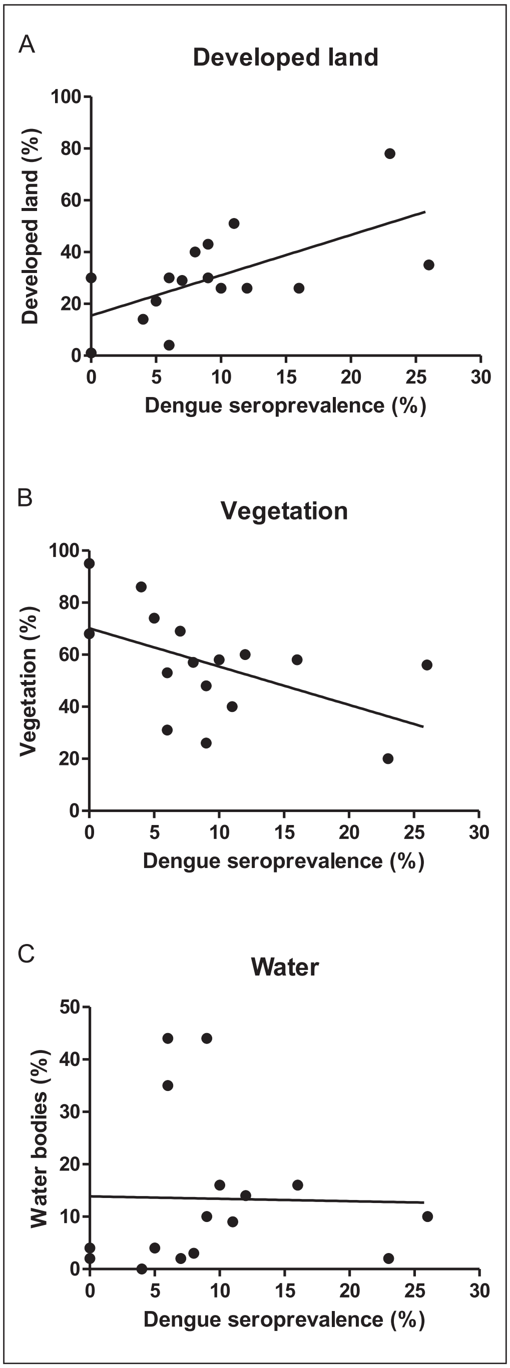

Figure 3. Graphical presentation of the relationship between dengue prevalence and the different land cover types: (A) land development, (B) vegetation and (C) water bodies.

DISCUSSION

The present study was undertaken to investigate the relationship between land cover variables and dengue seroprevalence in selected locations in Malaysia using the school children population and their respective school locations as the study sample and sites. Our findings suggest that dengue prevalence in school-going Malaysian children increases gradually with age, reaching ~16% of the study population between the ages of 16-18 years. Only less than 10% of those below 10 years had been exposed to dengue. Earlier reports by Hussin *et al.* (2005) and Jamaiah *et al.* (2005) suggested that dengue infection and mortality rates are higher in those above 15 years of age in Malaysia (Ministry of Health Malaysia, 2008). Similar observations were made in Vietnam (Thai *et al.*, 2005), Thailand (Simmons & Farrar, 2009) and Indonesia (Graham *et al.*, 1999). In contrast, Cambodia

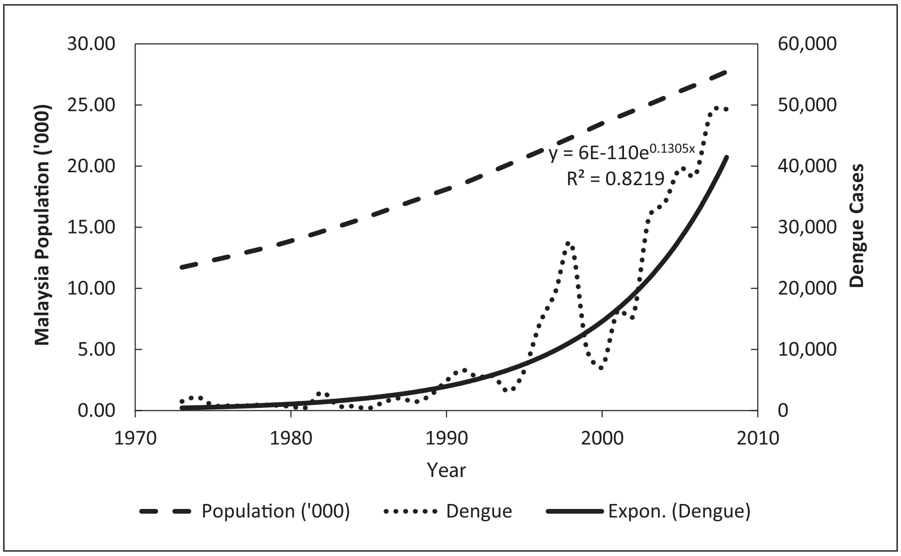

Figure 4. Population growth and dengue in Malaysia from 1973 to 2008.

reported a higher incidence among preschoolers (Vong *et al.*, 2010). In the Americas, in Venezuela and Mexico, dengue infections are more likely to occur among the 10-14 years age group, whereas it is more likely among young adults in Brazil and similar across all age groups in Honduras (Martin *et al.*, 2010). The findings presented here, hence, are consistent with the earlier reporting of the changing demography of those who are most likely to get dengue. It is thus, important to note that dengue infection is more likely to occur among older children in Malaysia. We speculate this may be that nowadays older children are more likely to engage in social groups and be more mobile than younger children. As such, they have a higher chance of coming into contact and contracting dengue from mosquito bites of other dengue-infected persons. Consequently, Reiner *et al.* (2014) have reported the effect that human movement has on the transmission of dengue.

Additionally, our findings suggest that land development, taken as a measure of the extent of urbanization, appears to be the best predictor of dengue prevalence among children compared to vegetation and water bodies. At least 70-80% of the reported cases in Malaysia were from the urban areas (Ministry of Health Malaysia, 2008). This was also observed in our study. The abundance of man-made containers, inadequate solid waste disposal and inadequate drainage system (Vanwambeke *et al.*, 2007) in urban areas are among the factors favoring *Ae. aegypti* breeding and transmission of dengue. High dengue incidences also occurred in areas with interconnected houses followed by mix housing type and independent housing type (Umor *et al.*, 2007). Mixed housing type consisted of both interconnected and independent houses. In our study, interconnected houses were the most common especially in the highly developed sites where dengue prevalence is also high except in KEL1 where the prevalence was highest, but the housing type was a mixture of interconnected houses and independent wooden houses. In KEL1, it is likely that other factors not measured in this study, such as socio-economic background (Wong *et al.*, 2014), water storing practices (Hairi *et al.*, 2003), and attitudes, practices and knowledge towards dengue (Wan Rozita *et al.*, 2006), may be more favored by dengue transmission. A high number of mosquito breeding places in the community were previously noted in Kota Bharu, the city where KEL1 is located (Hussin *et al.*, 2005), and this may also help to explain the higher prevalence of dengue among this study population.

We observed in our study that an increase in the prevalence of dengue in localities outside Selangor and Kuala Lumpur coincided with reduced land surface vegetation. This is consistent with the observation that in urban settings, high dengue prevalence occurs also mostly in the non-vegetated areas (Umor *et al.*, 2007). This is likely to be expected as less vegetation would coincide with increased human presence and activity and thus dengue transmission. At the same time, change in vegetation types like the clearing of forests for agriculture activities has been reported to favor the breeding of *Ae. aegypti* (Chang *et al.*, 1997). However, although not analysed in our study, in the microenvironment vegetation surrounding containers has been found to favor *Ae*. mosquito breeding (Kamgang *et al.*, 2013) likely by providing shelter.

In our study, the presence of large water bodies was a poor indicator of dengue prevalence. From the satellite imagery, only large water bodies such as lakes, wetlands and rivers could be clearly identified in all sites. These water bodies were usually at the outskirts of town or further and away from significant human presence. However, our results are in contrast with Cheong *et al.* (2014) who found that water bodies such as drains, lakes and rivers was found to be an important predictor of dengue cases. Nakhapakorn and Tripathi (2005) reported it to be significant in one district only out of nine in their study. The water bodies mentioned in our study may likely be poor mosquito breeding sites in comparisons to the numerous artificial containers found in urban areas (Saleeza *et al.*, 2011).

The current study is an initial approach in using remote sensing data and geographical land cover features to explore the potential significance of land cover types for assessing dengue seroprevalence. Our findings suggest that land cover type is an important factor to consider in dengue transmission and that urbanization marked by high land usage is strongly linked with the escalating dengue prevalence. This observation between land cover and dengue is also consistent with studies in Malaysia by Nazri *et al.* (2011), Cheong *et al.* (2014) and elsewhere (Nakhapakorn & Tripathi, 2005; Kannathasan *et al.*, 2013). In the current absence of effective dengue vaccine and therapeutics, further understanding of how urbanization contributes to higher dengue prevalence is of paramount importance. Here we suggest the importance of the built environment and spatial geographical features in dengue. Additionally, from our data, population density did not appear to be related to dengue prevalence. Schmidt *et al.* (2011) reported the highest risk of contracting dengue fever was in low-to-moderate population densities, although Araujo *et al.* (2014) found most dengue cases in highly populated areas although incidence was low in densely populated areas and vice versa. Nonetheless, we note that the number of dengue cases is increasing, as is the population of the country. Expectedly, with global population growth, climate change, the population at risk of contracting dengue has also been predicted to increase (Hales *et al.*, 2002).

Our study, however, is limited to only school children and only nine out of the fifteen Malaysian states and Federal Territories of Malaysia. Hence, this data set is limited in extrapolating to Malaysia's population. Also, for feasibility reasons, site visits were not performed which would have allowed us to confirm the land cover features observed in the satellite imagery. Site visits could also help us to further define the factors in developed land such as road access (Mahabir *et al.*, 2012), types of building or presence of water-holding containers as mentioned above. However, in another of our study by Wong *et al.* (2014), telephone interviews were conducted with households located in the same 26 school sites to investigate dengue seroprevalence and socio-demographic factors. Some of the findings included higher seroprevalence observed in participants living in high rise apartments and those with higher income although seroprevalence was reported to be higher in participants from rural areas. It is also possible the seroprevalence reported here may be underrepresented as dengue IgG levels may have dropped to undetectable levels in certain individuals post-infection. The absence of continuous antibody stimulation i.e. repeated exposure to dengue, however, may also reflect low endemicity of the virus in the locality although this has not been reported yet. Additionally, further studies on population growth, movement and behaviour would also provide further insight into the disease as these have been found to be key in understanding dengue transmission and vector behaviour (Gubler & Meltzer, 1999; Honório *et al.*, 2009; Stoddard *et al.*, 2009).

Acknowledgement. This study was supported in parts by University of Malaya (Research University Grant TA006-2008A and TA024-2009), Ministry of Science, Technology and Innovation (MOSTI), Malaysia's Genome Institute Initiative Grant (Grant no.: 07-05-MGI-GMB015) and the Ministry of Higher Education Long-Term Research Grant Scheme (LRGS), LRGS/TD/2011/UM/Penyakit-Berjangkit.

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