Global Patterns in Spatial Expansion of Dengue Serotype-I in Response to Increasing Surface Temperature

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Abstract

Dengue is a mosquito-borne viral infection (DENV serotypes 1-4) that imposes a serious health and economic burden in tropical and sub-tropical countries around the world. Increasing atmospheric temperature had changed the dynamics of the mosquito habitats and, thereby, influences distribution of these mosquito vectors. We examined the increase in the number of countries within the regions of Asia, Africa, and America's reporting laboratory confirmed dengue cases caused by DENV-1 as a response to increasing global surface temperature difference. Data on the number of countries with confirmed reports of dengue (Messina et al. 2014) and surface temperature difference (General Circulation Model) were subjected to scatter plots and linear regression. There were 113 recorded countries across three regions (America=44, comprising the North and South; Africa=28; and Asia=41) reporting dengue incidence from 1943 to 2013, of which 98 countries (America=41; Africa=20; and Asia=37 with the inclusion of Australia) reported confirmed dengue cases caused by DENV-1. Findings suggest that the effect of temperature to the expansion of dengue varies dramatically in certain groups of country. Here, we explore three patterns (PAT) of expansion response where 1) continuous increase in temperature results into a continuous increase in the number of countries with dengue cases (PAT-A), 2) initial increase in temperature results into increase in the number of countries with dengue cases but subsequent increase in temperature results in the decline of dengue expansion (PAT-B), and 3) initial increase in temperature results into higher rate of dengue expansion but continued increase slows it down (PAT-C). PAT-A represented the majority of these countries, including 10 out of 11 countries in Southeast Asia. These results are in congruence with the past studies that supports dengue expansion to be temperature-dependent.

Keywords: Dengue expansion, Surface temperature difference, Dengue virus serotype-1

1.0 Introduction

Dengue viruses (DENV) comprise four morphologically and phylogenetically-unique serotypes under genus *Flavivirus*, namely: DENV-1, DENV-2, DENV-3 and DENV-4 (Messina et al., 2014). Among these serotypes, DENV-1 is considered as the main circulating serotype which resulted in severe number of dengue cases and significant cause of morbidity throughout the world (Lambrechts et al., 2011). Furthermore, the predominant DENV-1 genotype had the capacity to produce various genotypes which resulted to different epidemic potential in majority of Asian and American countries (Nishiura et al., 2007; Morin et al., 2013; Messina et al., 2014).

Emerging dengue incidences are augmented by a number of factors such as population increase and unplanned urbanization which may result to outsized and crowded populations with substandard housing, poor sewage systems, inadequate water and improper waste disposal (Guzman and Kouri, 2003). As a result, escalating hospitalization and death have been a primary concern by healthcare practitioners to children and adult (Nishiura and Halstead, 2007). It can also be associated with climatic influences which hasten mosquito distribution, vector dynamics and human-mosquito interactions (Morin, Comrie, and Ernst, 2013). Dengue transmission is highly observed in endemic tropical areas (Johannson et al., 2009; Adams et al., 2010). However, studies have also elucidated cyclical patterns of continental virulence in areas with rainy season (Patz, 2003; Johannson et al., 2009; Adams et al., 2010), making the disease more endemic (Mousson et al., 2005). The transmission of dengue viruses is highly sensitive to climatic conditions based on several reasons. First, temperature changes affect vector-borne disease transmission and associated epidemic potential by altering the vector's reproductive rate, biting rate, the extrinsic incubation period of the pathogen, by shifting a vector's geographical range or distribution and increasing or decreasing vector-pathogen-host interaction and thereby affecting host susceptibility (Farnesi et al., 2009; Ibarra 2013; Messina et al., 2014). Second, precipitation also affects adult female mosquito density in moist and arid areas (Ibarra et al., 2013). An increase in temperature as well as precipitation leads to an abnormal increase in the available breeding sites which, in turn leads to an increase in mosquito density (Epstein, 1998; Keating, 2001; Stewart Ibarra, 2013). Studies have shown that climate variability influences dengue transmission and population dynamics worldwide, indicating the potential to develop public health interventions using climate information (Nishiura et al., 2007; Farnesi et al., 2009; Semenza and Menne, 2009; Naish et al., 2014).

While there is an increasing knowledge of the linkages between dengue serotype diseases and global surface temperature change, there is really a need to update such distribution patterns of dengue serotypes since these are potential factors in understanding population-risk factors for sever dengue illnesses and is also essential in understanding the overall viral pathogenicity and host genetics of dengue viruses to the human body (Naish et al., 2014). The need to focus on environmental and social factors, incorporated with assessment on vulnerability of water-health relationship, will be critical in addressing dengue incidence at a global scale (Morin et al., 2013). Moreover, the impacts brought by fluctuating global surface temperature on dengue distribution remain to be unclear. Further studies are yet to be conducted in order to analyze the relationship between global surface temperatures on the spatial distribution of dengue serotypes across the world (Lambrechts, 2011). Majority of the studies conducted have incipiently focused on the local and regional scales, which produce only minimal data (Sharmin, Glass, Viennet, and Harley, 2015). Global descriptions of type-specific DENV distribution, influenced by global surface temperature are few in number, making the study timely and relevant. Reported cases of dengue incidence associated with the influence of global surface temperature do not comprise the entire range of each DENV type at any given time and country, meaning that a lack of global reporting for a specific dengue serotype at any time, place and climatic influence does not indicate its certain absence (De Simone, 2004; Nishuira, 2007; Oehler, 2014). This is due to spatial variability in several factors, namely in the degree of sampling, proportion of infection having been typed individually, reliability of sampling and typing methods, and finally reporting these types and its climatic temperature (Morin et al., 2013; Messina et al., 2014).

Objectives of the study

The study will investigate the association between global annual surface temperature difference and the expansion of spatial distribution patterns of DENV-1. Moreover, this study will also determine association patterns that might be unique to any group of countries regarding the effect of increased temperature to the spatial distribution of dengue reports. Likewise, these patterns would be used to predict future trends in the proliferation of dengue incidences across the globe that will be needed in order to provide public health sectors worldwide with important information for future surveillance and monitoring of climatic-influenced dengue incidences, with the goal of reducing vector densities below an epidemic threshold.

Hypotheses of the study

In the study, the researchers hypothesized direct relationship between the increase in surface temperature and spatial expansion of dengue, that 1) the relationship between surface temperature and number of countries reporting dengue incidence shows direct proportionality through time; 2) as global temperature increases, the number of countries reporting dengue incidence caused by DENV-I also increases but gradually declined at certain point in time; and/ or 3) there is an increase in dengue incidence as the annual temperature difference increases, but the rate of increase is faster during the first half compared to the second half of the time period.

Conceptual Framework

Natural and human-induced activities can directly influence the spatial distribution patterns of dengue serotypes across the world. In turn, this can limit the abundance of dengue viruses in the environment. Suitable global annual surface temperature is considered to be one of the factors strongly associated with elevated prevalence of DENV-1. Through its multiple mechanisms, temperature is an important determinant of biting rate, time of development of DENV-1 serotype in the mosquito, development of eggs and immature mosquitoes, and its survival in all stages of the mosquito life cycle (Messina et al., 2014) and that global annual surface temperature affect the time between feeding and virus detection in the saliva of mosquitoes (Christophers, 1960). Furthermore, feeding behavior is also more frequent in increasing global annual surface temperatures, further affecting transmission risk. Monitoring of global surface temperature and identifying their possible trends can be helpful in assessing the distribution of dengue cases in different continents. External factors such as temperature could affect the prevalence and spatial distribution of dengue cases as presented below (Fig.1). Data on temperature have been noted. These data are essential in inducing the virulence of dengue virus via horizontal transmission and eventually affect the health status of humans. Applicable policies, standards and regulations can henceforth be implemented to control such spread of disease.

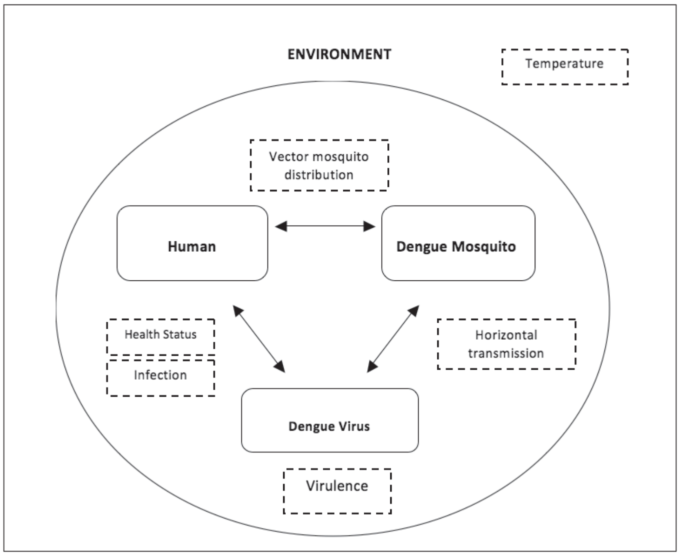

Figure 1. *Conceptual framework*

2.0 Materials and Methods

A seventy-year (1943-2013) data on global dengue reports by country were obtained from a study conducted by Messina et al. (2014), which were derived and, then, summarized from different published literatures and case reports from extensive databases such as PubMed, ProMED, and GenBank. Countries reporting dengue incidences caused by DENV-1 were initially categorized according to region: Asia, Africa, and Americas. Global surface temperature (in °C) were accessed online from General Circulation Model (GCM) developed by the National Aeronautics and Space Administration (NASA) Goddard Institute for Space Studies (GISS) which are made available to the public. Global surface temperature were linked with the global reports of DENV-1 through scatter plot diagrams and linear regression using Minitab software version 16.1. Patterns with high R-Sq value of more than 98% were then data mined from the original scatter plot. Countries being represented by each pattern were identified and the frequency of occurrence were determined. The best pattern or patterns to represent each country were determined by the highest frequency of occurrence observed.

3.0 Results and Discussions

There were 113 recorded countries across three regions (America=44, comprising the North and South; Africa=28; and Asia=41) reporting dengue incidence from 1943 to 2013, of which 98 countries (America=41; Africa=20; and Asia=37 with the inclusion of Australia) reported confirmed dengue cases caused by DENV-1 (Messina et al. 2014). Global trends of dengue incidence across countries had increased through time, where there were only less than five countries reporting dengue incidence due to DENV-1 serotype from 1943 to 1972 and has since increased drastically up to 2013 (Fig. 2). Likewise, separated data from the regions of Asia, Africa and Americas had shown a very similar trend from one another in the number of countries reporting dengue incidence from 1984 to 2012 (Fig. 3). Recently, dengue illness is known to burden and endemic in more than 125 countries across the globe (Murray, Quam, and Wilder-Smith, 2013).

Asia was the first one among the three regions to report dengue cases, specifically in Japan and French Polynesia, followed by the dengue reports in the Philippines in 1954 and India in 1956. Historical records suggest that the first recorded case of dengue was during the Chin dynasty around 992 AD (Gubler, 2006) and was referred to as 'water poison' (Murray, Quam, and Wilder-Smith, 2013). In 2002 and 2009, the highest number of countries with dengue was recorded, with 17 countries reporting confirmed dengue incidence by DENV-1 (Fig. 3). Since then, dengue reports had been documented in 37 countries in Asia and Oceania, including Australia. In 2011, World Health Organization (WHO) reported that out of 2.5 billion people at risk of dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS), about 1.3 billion (52%) people are coming from the South-East Asia (WHO, 2011).

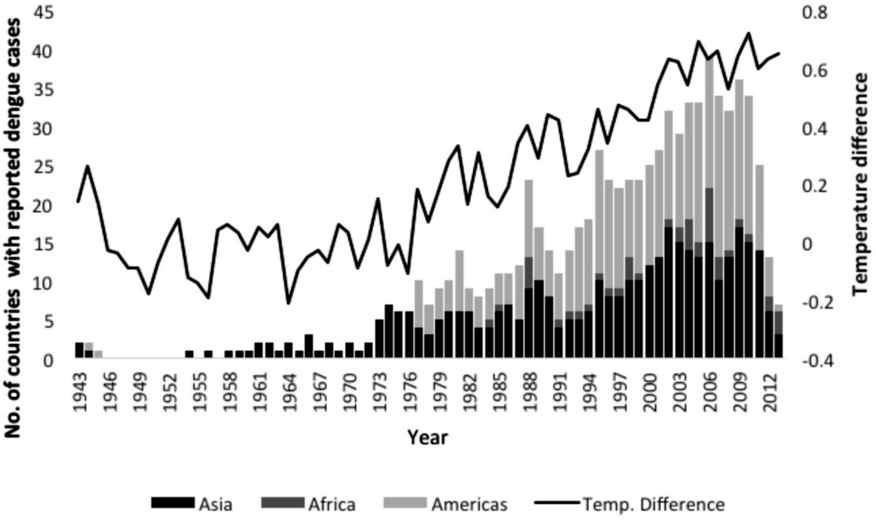

Figure 2. *Collective number of countries across Asia, Africa, North and South America showing dengue reports caused by DENV-1 from 1943 to 2013.*

History of dengue illness in the Americas can be presented into four main periods: 1) the introduction of dengue in the Americas (1600-1946); 2) eradication of vector mosquito *Aedes aegypti* (1947-1970); 3) vector mosquito reinfestation (1971-2000); and 4) increase dispersion and dengue virus circulation (2011-2010) (Dick et al., 2012). From the given data, United States of America was one of the first to confirm a dengue case caused by DENV-1 in 1944 where a new era of dengue research had paved way to viral isolation and diagnostic laboratory tests (Sabin and Schlesinger, 1945). There was a long period from 1946 to 1976 where there were no reports that had been documented in the Americas (Fig. 3). During this time after World War II, a collaborative effort to eliminate the dengue and yellow fever disease vector *Aedes aegypti* in the Americas took place, as initiated by the Pan American Health Organization (PAHO) from the early 1940s up to 1970 (Murray, Quam, and Wilder-Smith, 2013).The long hiatus has been broken with the emergence of dengue cases reported by the Bahamas, Cuba, French Antilles, French Guiana, and Puerto Rico in 1977. The year with the highest number of countries reporting dengue incidence was that of 2007.

In Africa, dengue cases were caused primarily by DENV-2, followed by DENV- 1 (Sang, 2006). Dengue reports in Africa had been very low due to the under-recognition of dengue in Africa resulting to lower rate of clinical reports and misdiagnosis of dengue illnesses (Amarasinghe et al., 2011). Malaria is highly endemic in Africa, more so than dengue illness, hence when individuals contracting fever of unknown cause in high malaria-risk places would automatically be report as malaria without confirmed laboratory diagnostics. Also, the so-called dengue resistance gene found in black population (Halstead et al., 2001) gives them certain immunity. Furthermore, monitoring and surveillance in Africa had been receiving little funding support with the assumption that dengue illness does not pose a significant health risk due to the lack of reported severe cases of dengue (Sang, 2006). Although the reports are quiet low, dengue illness in Africa had proved to be of significant economic and health burden (Bhatt, 2013). The data for dengue in Africa had documented the first report by Sudan in 1984, way later than that of Asia and the Americas, although dengue had been suggested to be introduced as far back as 1926 to 1927 in South Africa (Kokernot et al., 1956). In 2006, the highest number of countries reporting dengue incidence was recorded, where seven countries had been confirmed to have dengue cases caused by DENV-1, namely Burkina Faso, Cameroon, France-Mayotte, France-Reunion, Madagascar, Mali, and Saudi Arabia (Fig. 3).

There was a notable decrease in the collated number of countries reporting dengue incidence starting from 2010 until 2013. However, separate data of the three regions showed that Africa had an increase in the number of reporting countries from 2011 to 2013 as opposed to the trend found in the regions of Asia and Americas (Fig. 3). Although the number of countries reporting dengue incidence had been shown to increase up to 2009 and subsequently decreases thereafter, the average surface temperature difference had been continuously increasing through time. Climate change and the increasing trend of temperature in the past decades had been known to impose greater health risks to human population (Patz et al., 2005), most especially in the global expansion of dengue (Murray, Quam, and Wilder-Smith, 2013). Relationship between global surface temperature difference and the number of countries reporting dengue incidence suggests that an increase in temperature would result to a wide spread distribution of DENV-1 up to some point, but would eventually decrease with continuous increase in temperature.

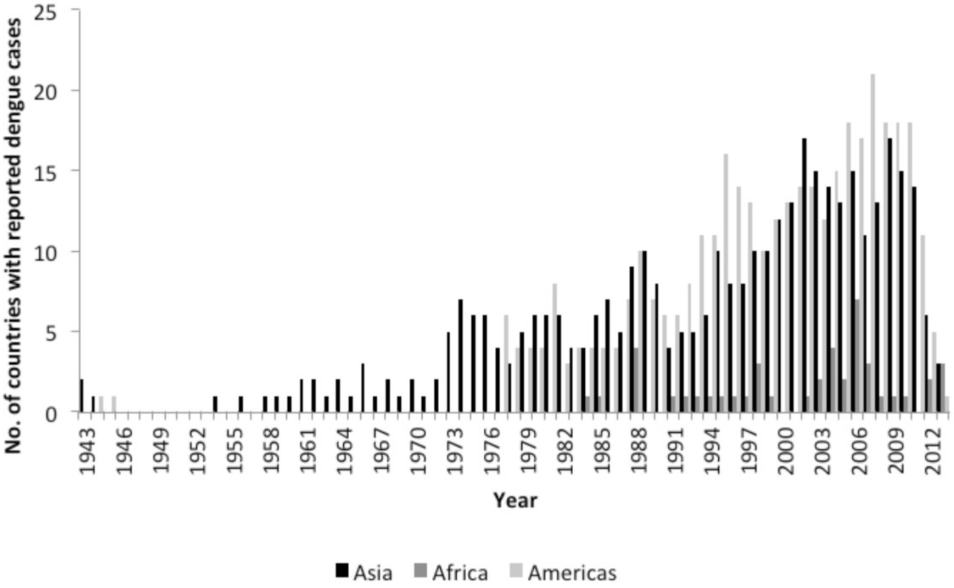

Figure 3. *Number of countries by continent (Asia, Africa, and Americas) reporting dengue incidence caused by DENV-1 from 1943 to 2013.*

The number of countries reporting confirmed cases of dengue and global surface temperature difference showed a direct proportionality with one another, with number of countries almost doubled with just a unit change of 0.4 in the global surface temperature (Fig. 4). Dengue transmission and vectorial capacity (VC) had been found to be highly influenced by temperature fluctuations and may limit levels of DENV endemicity (Brady et al., 2014). VC can be used to estimate dengue epidemic potential (DEP) which is shown to be highly temperature-dependence (Liu-Helmersson et al., 2014). This clearly shows the connection of the capacity of dengue vector mosquito to spatially disperse and its prowess in harbouring DENV to temperature. Diurnal temperature range (DTR), or the difference between the daily minimum and maximum temperature, plays a vital role in DENV transmission (Carrington et al., 2013), where prediction model at mean temperature less than 18˚C showed a direct proportionality between DENV transmission and DTR while at mean temperature greater than 18˚C, high DTR would negatively affect DENV transmission (Lambrechts et al., 2011). Since countries in different parts of the world had varying degree of DTR depending on its geographic location and climatic patters, this would create a different response on the spatial distribution of vector mosquito and its potential to cause an epidemic. This highly temperature-dependent transmission and spatial distribution of dengue mosquito would therefore generate different dengue proliferation patterns.

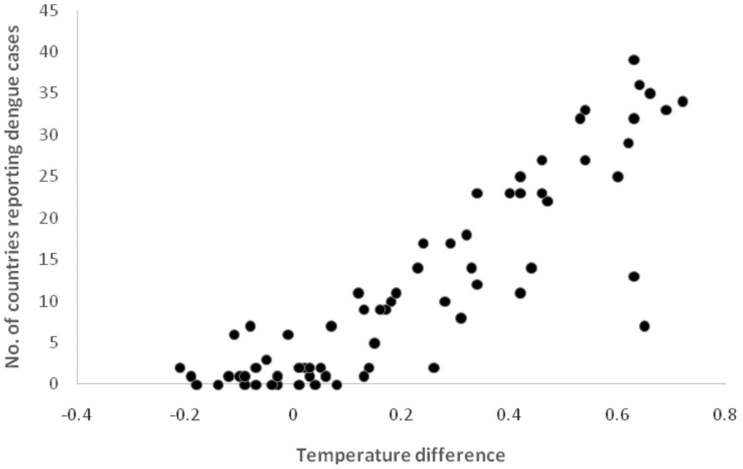

Figure 4. *Scatter plot of the number of countries reporting dengue incidence caused by DENV-1 and mean surface temperature difference from 1943 to 2013 with S = 5.55980 R-Sq = 77.8% R-Sq(adj) = 77.5%.*

Three regional patterns had been extracted from the scatter plot diagram where groups of several countries had shown unique proliferation of dengue in response to surface temperature differences: 1) Pattern A (PAT-A) wherein there is steady continuous increase in the number of countries with continuous increase in temperature (Fig. 5); 2) Pattern B (PAT-B) wherein there is an increase in the number of countries with an increase in temperature, but gradually decreases as temperature continuous to increase (Fig. 6); and 3) Pattern C (PAT-C) faster rate of increase in the number of countries with confirmed dengue with initial increase in temperature, but rate of increase gradually decrease with continued increase in temperature (Fig. 7). Out of the 113 countries, 75 countries had been represented by the three extracted patterns. PAT-A represented the majority of the countries (66 countries), followed by PAT-C (52 countries), then PAT-B (51 countries). There were countries that were represented by more than one pattern while few others were represented by only a single pattern. Countries unique to PAT-A are Anguilla, Antigua and Barbuda, Bhutan, Burkina Faso, Cameroon, Cote d'Ivoire, Dominican Republic, France-Reunion, France-Mayolte, Honduras, Madagascar, Mali, Micronesia, Nepal, Palau, Seychelles, St. Kitts and Nevis, and Saint Lucia. Moreover, 10 out of 11 countries in Southeast Asia (Cambodia, Timor Leste, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, Vietnam) obtained the highest frequency of occurrence in PAT-A. Brunei Darussalam had not been shown to be represented by any of the three patterns. Countries unique in PAT-B are only Samoa and Solomon Islands, which are both located near the equatorial zone. Countries unique in PAT-C includes the Bahamas, Belize, Cuba, Djibouti, Japan, Niue, US Virgin Island which are relatively located a little bit farther away from the equatorial zone. The representation of these countries through these patterns indicates the localized complexity of temperature-spatial distribution relationships. Countries represented by more than one pattern may have higher variability in temperature-spatial distribution relationship that might result to a rather difficult dengue vector distribution predictions in the future. On the other hand, those countries represented by only a single pattern be easier to predict the trend of vector distribution and temperature relationship.

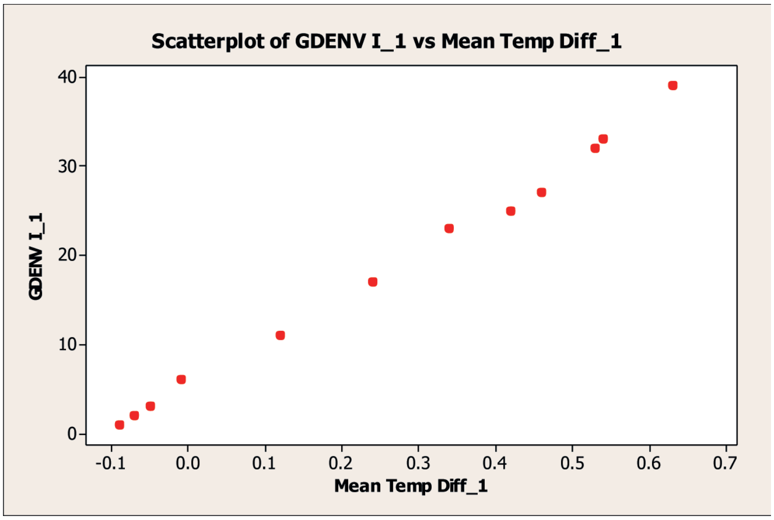

Figure 5. *Regional pattern of some countries plotted against increasing global temperature difference, showing a linear response in the number of reporting countries with confirmed cases of dengue caused by DENV-1 (S = 1.02244;R-Sq = 99.5%; adjusted R-Sq = 99.4%)*

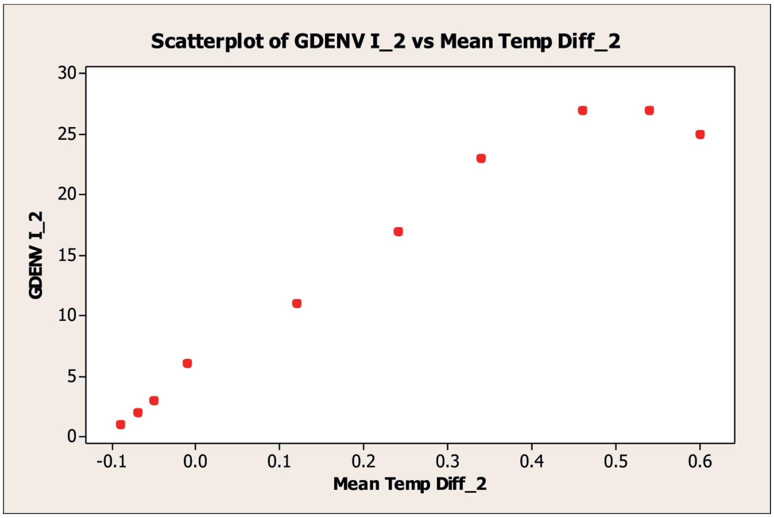

Figure 6.*Regional pattern of some countries plotted against increasing global temperature difference, showing initially a linear response in the number of reporting countries with confirmed cases of dengue caused by DENV-1, followed by a gradual decrease in the number of countries as the temperature continues to increase (S = 1.50011; R-Sq = 98.5%;adjusted R-Sq = 98.1%)*

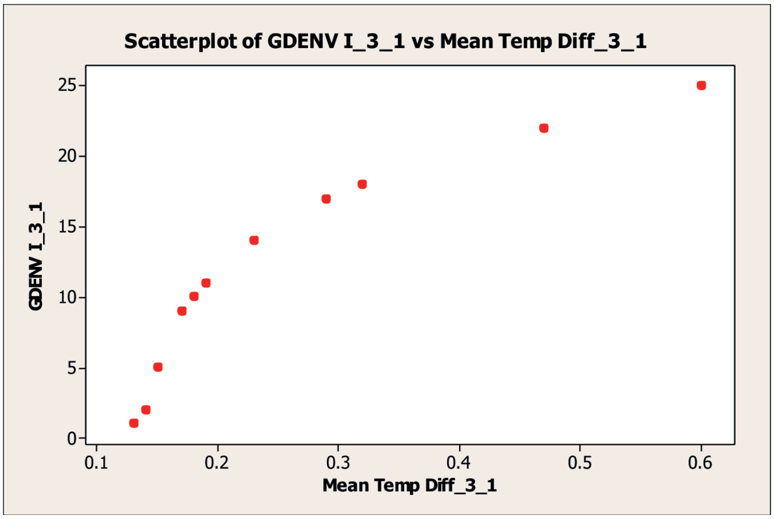

Figure 7. *Regional pattern of some countries plotted against increasing global temperature difference, showing initially a somewhat exponential response in the number of reporting countries with confirmed cases of dengue caused by DENV-1, followed by a gradually linear association in the number of countries as the temperature increases (S = 1.05564; R-Sq = 98.7%;adjusted R-Sq = 98.2%)*

Countries showing faster rate in dengue spatial expansion (PAT-C) and relatively constant rate of increase (PAT-B) with increase in surface temperature difference are mostly from the tropical region, where initial small differences in surface temperature had garnered an increase in the expansion of dengue in the region, as evident in the increase in the number of countries and with temperatures closer to 29˚C. These regional patterns generated in this paper had been highly in congruence to the finding of Liu-Helmersson et al. (2014), where slight change in the DTR in the tropics increases the DEP, while large changes in DTR can decrease the DEP. Greater difference in the surface temperature had resulted to a slower expansion rate of dengue in PAT-C and a decrease in the expansion of dengue in PAT-B. This finding stresses on the epidemic potential of the dengue vector as it changes its spatial distribution in response to temperature. Higher temperatures (20-30°C) facilitate proliferation of the virus inside the vector's body and yield the highest viral titer (Alto and Bettinardi, 2013) and thus increase also its potential for dengue transmission. In Singapore, higher mean temperature coupled with high cumulative precipitation from 2004 to 2007 had been reported to be a cause of the increase intensity and magnitude of dengue cases in the country (Hii et al., 2009). In the temperate regions, increase DTR results also to higher DEP, which would mean that when temperature from the temperate countries fluctuate heavily away from the cooler mean temperature relative to that of the tropics, spatial distribution as well as dengue transmission increased in magnitude. PAT-A had been very similar in this regard. Furthermore, projections for the DEP in the northern hemisphere is said to have large increases to be expected at the end of the 21st century. This finding farther proves that increased temperature of cooler temperate countries as a result of global warming will also expand the endemicity of dengue around the world.

Temperature-dependent dengue expansion patterns might prove to be highly important in the monitoring and surveillance of dengue vectors as well as for the use as a basis for predictions in future epidemic episodes of a country of a certain region. Dengue predictions provide early warning system before a prospective outbreak can occur and may increase effectiveness of preventive measures (Hii et al. 2012; Cheong et al., 2013; Ramachandran et al., 2016; Choi et al., 2016). In the dengue endemic countries like the Philippines, predictive modelling studies such as this ensures local health offices to have ample amount of time to create preventive plans in the future (Buczak et al., 2014). Though predictions are very helpful in this regard, this should also be coupled with integrated and community-based dengue vector control and surveillance to substantially reduce vector population and dengue incidences in the future (Edillo, Roble and Otero II, 2012; Liaqat, Jahan and Ahmad, 2013).

4.0 Conclusion

Global expansion of dengue is highly temperature-dependent. Patterns of dengue expansion in response to global temperature difference vary from one region to another. Countries in the subtropical and temperate zone is highly susceptible to dengue expansion during large increase in temperature while that of tropical zone might experience an increase in transmission and vector distribution as mean surface temperature increases but might also experience a decrease in dengue expansion depending on the daily temperature range of the place. Thus it is highly recommended to include data on diurnal temperature range in future studies to further highlight the importance of temperature in the regional expansion of dengue. Also, global dengue expansion cannot solely be attributed to temperature rise alone. Urbanization, high population density, and easy accessibility to transport can also be implicated and therefore needs to be looked into together with climatic and other environmental factors.

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