Tropical Biomedicine 29(4): 499–507 (2012)

Potential impacts of climate variability on Dengue Hemorrhagic Fever in Honduras, 2010

Zambrano, L.I.[1], Sevilla, C.[1], Reyes-García, S.Z.[1], Sierra, M.[2], Kafati, R.[3], Rodriguez-Morales, A.J.[4,5,6,7,*] and Mattar, S.[6,8]
[1]Hospital Escuela, Faculty of Medical Sciences, Universidad Nacional Autónoma de Honduras (UNAH), Tegucigalpa, Honduras
[2]Scientific Research Unit, Faculty of Medical Sciences, Universidad Nacional Autónoma de Honduras (UNAH), Tegucigalpa, Honduras
[3]Department of Epidemiology, Hospital Escuela, Secretary of Public Health, Tegucigalpa, Honduras
[4]Research Group Infection and Immunity, Faculty of Health Sciences, Universidad Tecnológica de Pereira (UTP), Pereira, Risaralda, Colombia
[5]Office of Scientific Research, Cooperativa de Entidades de Salud de Risaralda (COODESURIS), Pereira, Risaralda, Colombia
[6]Committee on Zoonoses and Hemorrhagic Fevers of the Colombian Association of Infectious Diseases (Asociación Colombiana de Infectología, ACIN), Bogotá, Colombia
[7]Instituto Experimental José Witremundo Torrealba, Núcleo Universitario Rafael Rangel, Universidad de Los Andes, Trujillo, Venezuela
[8]Instituto de Investigaciones Biológicas del Trópico, Universidad de Cordoba, Montería, Cordoba, Colombia
[*]Corresponding author email: arodriguezm@utp.edu.co
Received 21 March 2012; received in revised form 30 July 2012; accepted 31 July 2012

Abstract. Climate change and variability are affecting human health and disease direct or indirectly through many mechanisms. Dengue is one of those diseases that is strongly influenced by climate variability; however its study in Central America has been poorly approached. In this study, we assessed potential associations between macroclimatic and microclimatic variation and dengue hemorrhagic fever (DHF) cases in the main hospital of Honduras during 2010. In this year, 3,353 cases of DHF were reported in the Hospital Escuela, Tegucigalpa. Climatic periods marked a difference of 158% in the mean incidence of cases, from El Niño weeks (-99% of cases below the mean incidence) to La Niña months (+59% of cases above it) ($p<0.01$). Linear regression showed significantly higher dengue incidence with lower values of Oceanic Niño Index ($p=0.0097$), higher rain probability ($p=0.0149$), accumulated rain ($p=0.0443$) and higher relative humidity ($p=0.0292$). At a multiple linear regression model using those variables, ONI values shown to be the most important and significant factor found to be associated with the monthly occurrence of DHF cases ($r^2=0.649$; $\beta_{standardized}=-0.836$; $p=0.01$). As has been shown herein, climate variability is an important element influencing the dengue epidemiology in Honduras. However, it is necessary to extend these studies in this and other countries in the Central America region, because these models can be applied for surveillance as well as for prediction of dengue.

INTRODUCTION

Dengue fever continues to be the most important vector-borne viral disease in the world. Its burden affects particularly poor urban, suburban and rural areas in South East Asia and Latin America. In this last continent, the re-emergence and subsequent failure to control the disease have provided a compelling illustration of the clinical, political and socio-economic challenges to eradicating it across the world (Tapia-Conyer *et al.*, 2009).

Dengue fever and dengue hemorrhagic fever (DHF) have reemerged and are increasing in Latin American countries, even in those previously certified as free of *Aedes aegypti* (Guzman & Kouri, 2003). These conditions, particularly DHF (the severe manifestation of dengue infection characterized by multiple hemorrhages, and potentially followed by circulatory failure, neurological manifestations, and shock) can produce a significant disease burden, expressed in terms of premature mortality (years of life lost, or YLLs) and disability (years of life lived with a disability, weighted by the severity of the disability, or YLDs) (Mathers *et al.*, 2007).

Given that emergence and resurgence can be attributed to multiple factors including urbanization, transportation and changes in human migration and behavior, resulting in its increase as the second most important vector-borne disease after malaria, in terms of human morbidity and mortality (Gubler 1998; Mackenzie *et al.*, 2004). Difficulties with diagnosis, asymptomatic infection and the lack of effective surveillance systems account for the discrepancies between antibody prevalence against dengue and reported cases. Accurate incidence data and appreciation of the economic impact of dengue at regional, national and international levels are essential in securing political and economic commitment for dengue control efforts as well as increased scientific and social awareness (Tapia-Conyer *et al.*, 2009).

In addition, environmental control efforts require an integrated and systematic approach at both the national and community level, while successful introduction of a dengue vaccine will require an educational programme that clearly communicates the cost-effectiveness and desirability of this interventional measure (Tapia-Conyer *et al.*, 2009), particularly in the context of global warming and climate variability on disease.

All those complex interacting factors can be influenced by climate, as the ecological niches of the vector, *A. aegypti*, can be favoured and then its population able to transmit disease can increase significantly (Cassab *et al.*, 2011). Different studies have implied that cold temperature can limit its lifecycle, rather then acting as an influencing factor on its distribution (Beebe *et al.*, 2009), however, the role of ambient temperature on the transmission of dengue has been underscored in several studies (Chowell & Sanchez, 2006; Earnest *et al.*, 2012; Hu *et al.*, 2012; Wu *et al.*, 2012).

Studies in different parts of the world have evidenced (Hii *et al.*, 2009; Morales Vargas *et al.*, 2010; Wilson *et al.*, 2011; Thai & Anders, 2011; Bush *et al.*, 2011), particularly in South East Asia, that climate change and variability significantly influence the epidemiology of dengue. However, few studies from Latin America have evidenced its regional importance (Camara *et al.*, 2009; Herrera-Martinez & Rodriguez-Morales 2010; Chowell *et al.*, 2011; Colon-Gonzalez *et al.*, 2011).

For these reasons, in this study we assessed potential associations between macroclimatic and microclimatic variation and dengue cases in the major hospital of Honduras, where no previous studies on climate variability has been published, during a year with high incidence and epidemic of disease (2010). Honduras and Central America and the Caribbean region have been neglected in research on climate variability and dengue.

MATERIALS AND METHODS

Hospital Escuela, Tegucigalpa, Honduras, is the main general university hospital of the country. The Department of Epidemiology is in charge of surveillance and laboratory confirmatory follow-up of all patients suspected with dengue. This is registered in a daily basis.

For this study, the epidemiological data was constituted by all the daily records of confirmed dengue cases in children and adults diagnosed during the period 1 January 2010 till 31 December 2010. Diagnosis was initially clinically made and then serologically (ELISA) and virologically (viral isolation) confirmed by the reference public health laboratory system, according to the national control program for dengue fever of the Ministry of Health. Before the year 2010 epidemics, no accurate records of dengue were available. For these reasons, no previous data could be included for analyses.

The climatic data was based on one global macroclimatic index, the Oceanic Niño Index (ONI), classifying the climatic periods according to National Oceanographic and Atmospheric Administration (NOAA, USA) classification, and months were categorized as El Niño, Neutral and La Niña to establish differences in the dengue incidence according to those climatic periods. Additionally, microclimatic variables analyzed for the period included accumulated rain (mm), maximum temperature (ºF), minimum temperature (ºF), monthly rain probability (%), relative humidity (%), sun hours (hours/day), obtained from databases of the National Meteorological Service of the country and the PWS Network of meteorological stations in the country (IBAYISLA2, ICORTEST2 and IROATANB2).

Monthly satellite images for total rainfall were obtained from the Tropical Rainfall Measuring Mission (1 month - TRMM) imagery database NASA Earth Observations (NEO, NASA, USA) (http://neo.sci.gsfc.nasa.gov/) and analyzed for Honduras with the software Google Earth®.

Statistical analysis

Descriptive statistics were generated for the epidemiological and climatic data (means, standard deviations, SD). Qualitative and quantitative comparisons were made for climatic periods. Linear regression models were used for determining potential associations between the climatic and the epidemiological variables analyzed at monthly level (Table 1). Statistical significance was defined as $p<0.05$. Statistical analyses were performed on GraphPad Prism v.5.0®.

RESULTS

During the study period, 3,353 cases of DHF were diagnosed and reported. The mean number of dengue cases per month was 279±455 (±SD), while the mean number of dengue cases per week was 70±114 (range 0-130 cases/week) and per day was 17±17 (range 0-70 cases/week) (Figure 1).

During the considered climatic periods, a net difference of 157.62% was observed

Table 1. Monthly report of Dengue Hemorrhagic Fever Cases in the Hospital Escuela, Tegucigalpa, Honduras and the monthly climatic variables for Honduras, 2010, including the univariate analysis of the relationship of those elements with cases (using linear regression models)

		Climatic Variables					
Month	Cases	ONI	Accumulated rain (mm)	Monthly rain probability (%)	Relative humidity (%)	Minimal Temperature (ºF)	Maximal Temperature (ºF)
January	3	1.7	259	1.7	71	59	79
February	2	1.5	299	1.5	65	61	82
March	4	1.2	553	1.2	59	61	86
April	6	0.8	587	0.8	57	63	88
May	71	0.3	805	0.3	66	66	86
June	606	-0.2	891	-0.2	75	66	82
July	1432	-0.6	891	-0.6	76	64	82
August	839	-1	955	-1	74	64	84
Linear	r^2	0.6989	0.5173	0.6556	0.5751	0.2049	0.06498
regresions	p	0.0097	0.0443	0.0149	0.0292	0.2600	0.5424

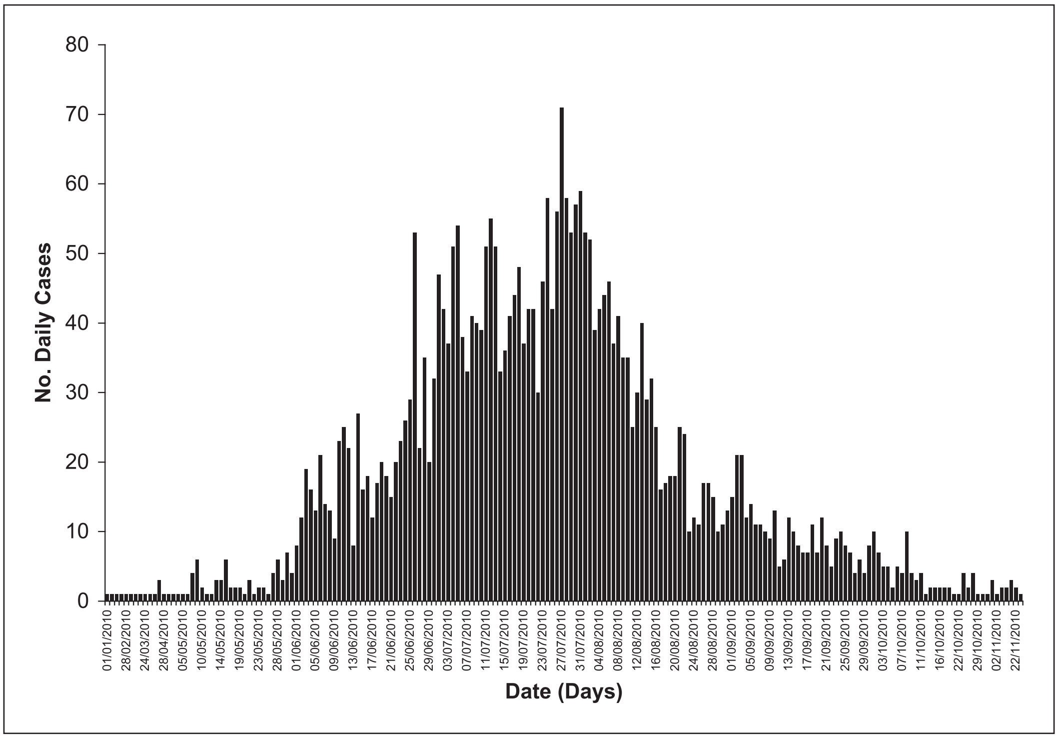

Figure 1. Daily report of Dengue Hemorrhagic Fever Cases in the Hospital Escuela, Tegucigalpa, Honduras, 2010

in the mean incidence of cases, from El Niño weeks (-98.66% of cases below the mean incidence) to La Niña months (+58.96% of cases above the mean incidence) (χ^2=27.91; p<0.01) (Figure 2). These patterns at macroclimatic indicators were consistent with the observation of the changes in the rain patterns in Honduras, which begin in 2010 with a dry season and few rain (<200 mm) in January (as expected for El Niño weeks) up to a rainy season (>200 mm) in the months of June, July and August (as expected for La Niña weeks) (Figure 3), and in coincidence with the highest peak of DHF daily incidence records (Figure 1).

Linear regressions between the ONI index, monthly rain probability, accumulated rain, relative humidity, and the dengue incidence showed a significant association (p<0.05). With lower values of ONI (below 0, La Niña periods) higher incidence of dengue was observed (r^2=0.6989; F=13.93; p=0.0097) (Figure 4A). Similarly, a higher rain probability (%) was significantly associated with a higher incidence of dengue (r^2=0.6556; F=11.42; p=0.0149) (Figure 4B). Accumulated rain was also a significant positive association with the dengue incidence (r^2=0.5173; F=6.43; p=0.0443) (Figure 4C). Finally, higher relative humidity also had a significant association with dengue incidence (r^2=0.5151; F=8.121; p=0.0292) (Figure 4D). Other variables analyzed, such as maximum temperature, minimum temperature and monthly rain sun hours were not significantly associated with the dengue incidence (p>0.05) (Table 1).

Finally, a multiple linear regression model for predicting monthly cases of DHF, using relative humidity, accumulated rain, rain probability and ENSO ONI values was analysed. At this model ENSO ONI values shown to be the most important and significant factor found to be associated with the monthly occurrence of DHF cases (Table 2).

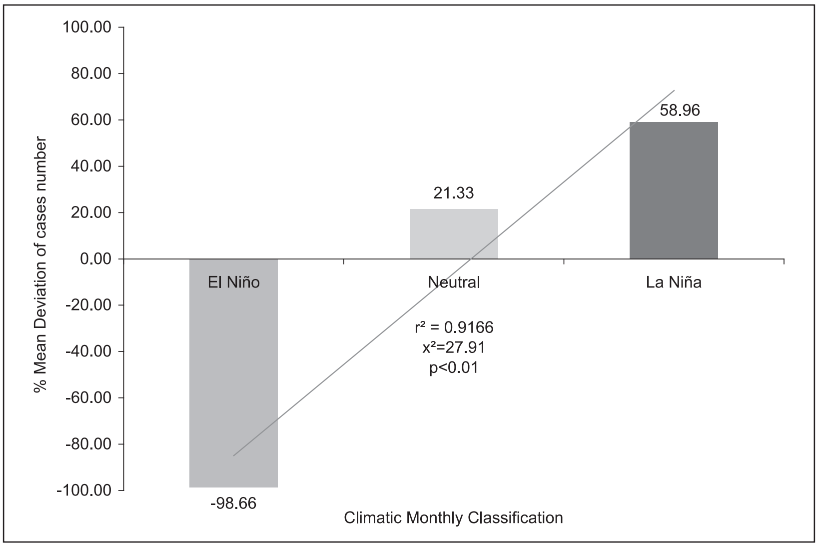

Figure 2. Difference in the mean incidence of DHF cases, from El Niño and La Niña months, Hospital Escuela, Tegucigalpa, Honduras, 2010

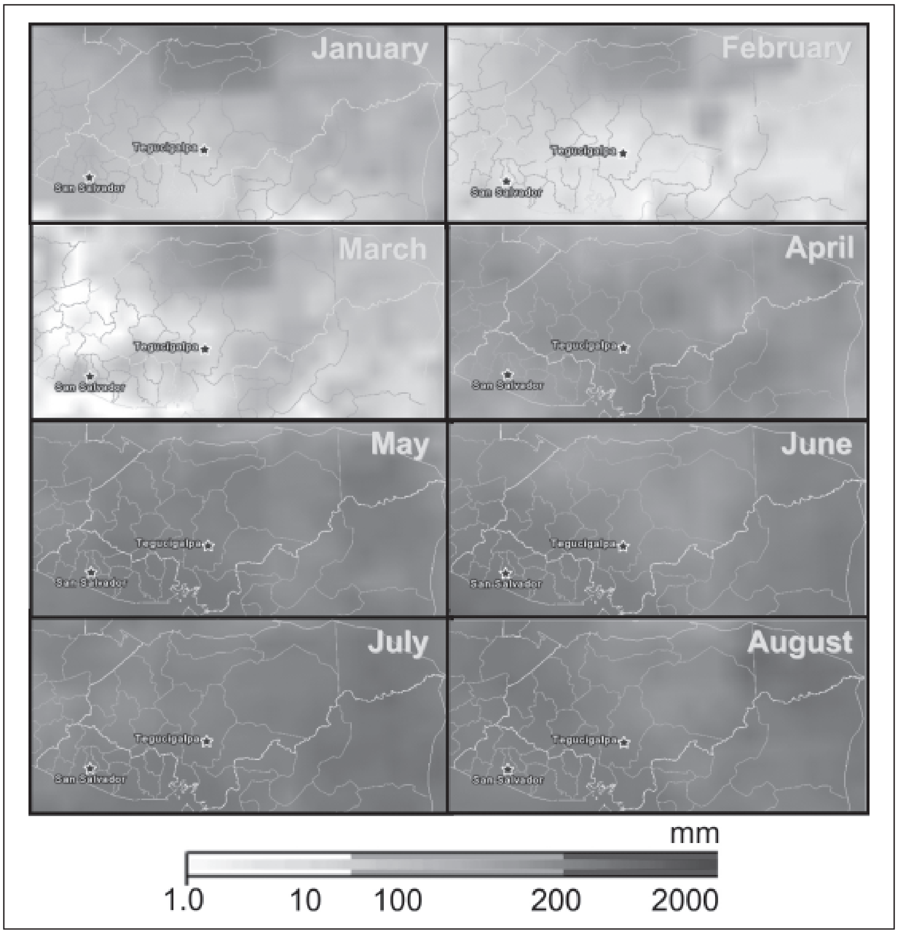

Figure 3. Rain patterns maps from the TRMM satellite for Honduras during January to August 2010 (NEO/NASA)

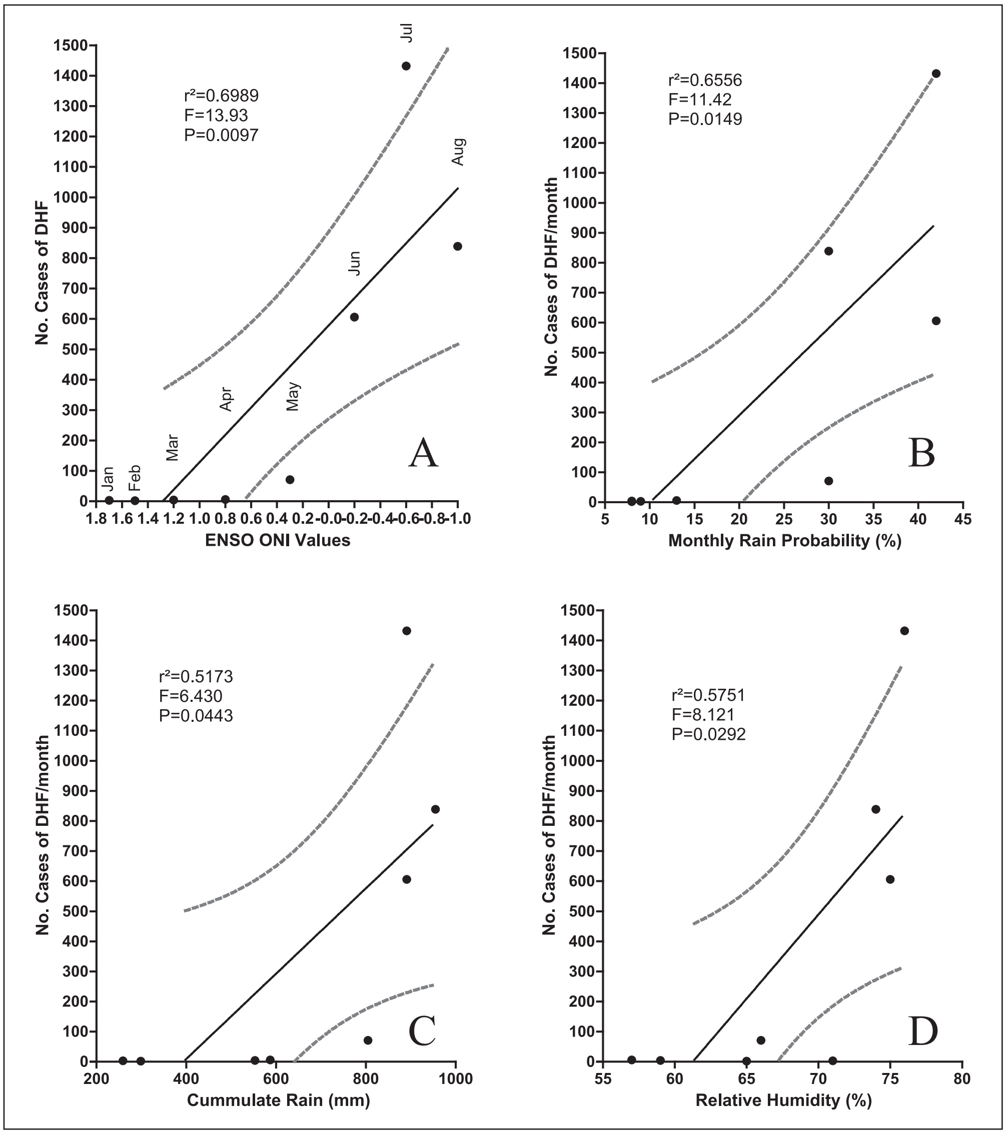

Figure 4. Relationship between macro and microclimatic variables and the monthly records of Dengue Hemorrhagic Fever Cases in the Hospital Escuela, Tegucigalpa, Honduras, January-August, 2010. A. ENSO climate variability indicator ONI. B. Monthly rain probability (%). C. Accumulated rain (mm). D. Relative humidity (%)

Table 2. Summary of the multiple linear regression models for predicting monthly cases of DHF, using relative humidity, accumulated rain, rain probability and ENSO ONI values

r	r^2	Adjusted r^2	Std. Error of the Estimate	Change Statistics: r Square Change	F Change	df1	df2	p
0.836	0.699	0.649	319.11	0.699	13.929	1	6	0.01
	Unstandardized Coefficients		Standardized Coefficients				95,0% Confidence Interval for β	
ENSO ONI Values	β	Std. Error	β		t	p	Lower Bound	Upper Bound
	-450.193	120.625	-0.836		-3.732	0.01	-745.351	-155.035

DISCUSSION

Dengue continues to be one of the most important vector-borne and tropical diseases around the world, affecting significantly many countries at South East Asia and Latin America. Dengue virus transmission dynamic can also be affected by the climate and its variability and extreme anomaly phenomena such as El Niño Southern Oscillation (ENSO), which is a profound incident in Latin America, particularly in countries with Ocean Pacific coasts, such as Peru, Ecuador or Panama and Honduras, as with many others in Central America.

The ENSO phenomena is considered a periodic change in the atmosphere and ocean of the tropical Pacific region, manifested in the atmosphere by changes in pressure and in the ocean by warming or cooling of sea surface at the tropical Eastern Pacific Ocean. In South America, its effects on tropical diseases, including dengue have been well documented (Herrera-Martinez & Rodriguez-Morales 2010; Chowell *et al.*, 2011), however in Central America few studies have linked ENSO to tropical diseases incidence and epidemics, e.g. in Costa Rica (Chaves *et al.*, 2008; Fuller *et al.*, 2009). Up to date there have been no studies in Panama, Nicaragua, El Salvador, Belize, and Guatemala, and this is the first report from Honduras linking ENSO and climatic variation to dengue incidence and epidemics.

ENSO phenomena measurement has been proven to be useful in dengue epidemiology through the use of Oceanic Niño Index (ONI) when modeling as one of the independent factors affecting the dynamics of case incidence (Rifakis *et al.*, 2005; Herrera-Martinez & Rodriguez-Morales, 2010). ENSO has two main phases that constituted the phenomena, El Niño, the period when water in the Pacific region is warmer than the means (of the temperature during the previous period) while La Niña is the period when the water is colder than the means (of the temperature during the previous period). These periods could be measured by the ONI, positives values indicating El Niño phase and negative values La Niña phase (Figure 2). In this study, as in others previously reported (Rifakis *et al.*, 2005; Herrera-Martinez & Rodriguez-Morales, 2010), La Niña phase was significantly associated with an increase of dengue incidence (Figure 2 and 4). However, in this study from Honduras the net change between El Niño and La Niña phase was much higher (157.62%) than that reported in western Venezuela during 2001-2008 (23.15%). Differently from the methodology used in that study, incorporation of microclimatic variables in this study found consistency with the macroclimatic influence of ENSO over the dengue epidemiology in Honduras.

These results would be explained by the existence of environmental conditions influenced by that macroclimatic change favorable for *Ae. aegypti* reproduction in Tegucigalpa, particularly in the context of urban climatic change (Sutherst, 2004), and although this is one-site dengue epidemiology study, given the geographical extension of the country, would reflect the country's influence of climate on dengue epidemiology.

La Niña in Honduras has influenced microclimatic conditions such as increase in the rainfall, humidity and lowering temperatures (Figure 3). However, temperature variability in Honduras did not change significantly over the study period (low variability) and was not significantly associated with dengue incidence (Table 1). Further studies using longer time series of dengue incidence are needed.

In any case, rainfall increase the collections of water at any type of waterholding container in urban settings (tree holes or leave as well as man-made cisterns, discarded bottles and tires), which are suitable for the laying of eggs by *Ae. aegypti*, making these favorable conditions breeding habitats for the mosquito and increasing the available population of vector for the dengue viruses to be transmitted to human beings. For these reasons, prospective collection of data on dengue is being recorded in order to improve the analyses on the potential relationships between the ENSO changes, as was observed in our current study, and the change in dengue cases at the same time.

Despite the limitations of our study (e.g. lack of vegetation data, such as NDVI or EVI, short-time data series, data used here comes from a single El Nino to La Nina transition period and can not reflect trends for multiple events), results shown that in this 1-year study more than 98% of reduction of disease mean incidence was observed during El Niño (dry season), and with La Niña (wet season) almost 59% of increase was observed, which would be further modeled and extended with longer time series of data, more reliable, in order to develop predictive models. Furthermore, it is necessary to extend the deepness of these studies in this and other countries in the region, because these models, with longer data and other variables, can be applied to surveillance data for predicting trends in dengue incidence in this and other Central American countries (Fuller *et al.*, 2009). In order to improve these analyses, on the effect of a variable that changes on a multi-year scale, other drivers of dengue should be also considered (Colon-Gonzalez *et al.*, 2011).

These results linking potential impacts of climate variability with dengue epidemiology should be considered in public health policies, particularly those focused on surveillance, forecast and prediction of disease.

Acknowledgements. This manuscript has been previously presented in part at the X Congreso Científico ASOCEM-UNAH 2011 - Encuentro Centroamericano SOCEMs (X Scientific Congress of the Scientific Association of Medical Students, ASOCEM, of the Universidad Nacional Autónoma de Honduras, UNAH, 2011 – Centroamerican Meeting of Medical Students' Scientific Societies), Tegucigalpa, Honduras, November 23-26, 2011 (Oral presentation). Also presented in part orally at the VIII National Meeting of Research on Infectious Diseases of the Colombian Association of Infectious Diseases (ACIN), May 2012, Armenia, Quindío, Colombia and at the XV Congress of Medicine of the Universidad Dr. José Matías Delgado "Dr. Benjamín Ruiz Rodas", May 2012, San Salvador, El Salvador (awarded there with the first place in the category post-graduate, VI Research Prize TERAMED).

REFERENCES

Beebe, N.W., Cooper, R.D., Mottram, P. & Sweeney, A.W. (2009). Australia's dengue risk driven by human adaptation to climate change. *PLoS Neglected Tropical Diseases* **3**: e429.

Bush, K.F., Luber, G., Cota, S.R., Dhaliwal, R.S. & Kapil, V. (2011). Impacts of climate change on public health in India: future research directions. *Environmental Health Perspectives* **119**: 765-770.

Camara, F.P., Gomes, A.F., Santos, G.T. & Camara, D.C. (2009). Climate and dengue epidemics in State of Rio de Janeiro. *Revista da Sociedade Brasileira de Medicina Tropical* **42**: 137-140.

Cassab, A., Morales, V. & Mattar, S. (2011). Factores climáticos y casos de dengue en Montería, Colombia. 2003-2008. *Revista de Salud Publica (Bogotá)* **13**: 115-128.

Chaves, L.F., Cohen, J.M., Pascual, M. & Wilson, M.L. (2008). Social exclusion modifies climate and deforestation impacts on a vector-borne disease. *PLoS Neglected Tropical Diseases* **2**: e176.

Chowell, G. & Sanchez, F. (2006). Climate-based descriptive models of dengue fever: the 2002 epidemic in Colima, Mexico. *Journal of Environmental Health* **68**: 40-44.

Chowell, G., Caselles, B., Broutin, H. & Munayco, C.V. (2011). The influence of geographic and climate factors on the timing of dengue epidemics in Peru, 1994-2008. *BMC Infectious Diseases* **11**: 164.

Colon-Gonzalez, F.J., Lake, I.R. & Bentham, G. (2011). Climate variability and dengue fever in warm and humid Mexico. *American Journal of Tropical Medicine and Hygiene* **84**: 757-763.

Earnest, A., Tan, S.B. & Wilder-Smith, A. (2012). Meteorological factors and El Niño Southern Oscillation are independently associated with dengue infections. *Epidemiology and Infection* **140**: 1244-1251.

Fuller, D.O., Troyo, A. & Beber, J.C. (2009). El Nino Southern Oscillation and vegetation dynamics as predictors of dengue fever cases in Costa Rica. *Environmental Research Letters* **4**: 140111-140118.

Gubler, D.J. (1998). Resurgent vector-borne diseases as a global health problem. *Emerging Infectious Diseases* **4**: 442-450.

Guzman, M.G. & Kouri, G. (2003). Dengue and dengue hemorrhagic fever in the Americas: lessons and challenges. *Journal of Clinical Virology* **27**: 1-13.

Herrera-Martinez, A.D. & Rodriguez-Morales, A.J. (2010). Potential influence of climate variability on dengue incidence registered in a western pediatric Hospital of Venezuela. *Tropical Biomedicine* **27**: 280-286.

Hii, Y.L., Rocklov, J., Ng, N., Tang, C.S., Pang, F.Y. & Sauerborn, R. (2009). Climate variability and increase in intensity and magnitude of dengue incidence in Singapore. *Global Health Action* **2**: 10.3402/gha.v2i0.2036.

Hu, W., Clements, A., Williams, G., Tong, S. & Mengersen, K. (2012). Spatial patterns and socioecological drivers of dengue fever transmission in Queensland, Australia. *Environmental Health Perspectives* **120**: 260-266.

Mackenzie, J.S., Gubler, D.J. & Petersen, L.R. (2004). Emerging flaviviruses: the spread and resurgence of Japanese encephalitis, West Nile and dengue viruses. *Nature Medicine* **10**: S98-S109.

Mathers, C.D., Ezzati, M. & Lopez, A.D. (2007). Measuring the burden of neglected tropical diseases: the global burden of disease framework. *PLoS Neglected Tropical Diseases* **1**: e114.

Morales Vargas, R.E., Ya-Umphan, P., Phumala-Morales, N., Komalamisra, N. & Dujardin, J.P. (2010). Climate associated size and shape changes in *Aedes aegypti* (Diptera: Culicidae) populations from Thailand. *Infection, Genetics and Evolution* **10**: 580-585.

Rifakis, P., Gonçalves, N., Omaña, W., Manso, M., Espidel, A., Intingaro, A., Hernández, O. & Rodríguez-Morales, A.J. (2005). Asociación entre las Variaciones Climáticas y los Casos de Dengue en un Hospital de Caracas, Venezuela, 1998-2004. *Revista Peruana de Medicina Experimental y Salud Publica* **22**: 183-190.

Sutherst, R.W. (2004). Global change and human vulnerability to vector-borne diseases. *Clinical Microbiology Reviews* **17**: 136-173.

Tapia-Conyer, R., Mendez-Galvan, J.F. & Gallardo-Rincon, H. (2009). The growing burden of dengue in Latin America. *Journal of Clinical Virology* **46 Suppl 2**: S3-S6.

Thai, K.T. & Anders, K.L. (2011). The role of climate variability and change in the transmission dynamics and geographic distribution of dengue. *Experimental Biology and Medicine* **236**: 944-954.

Wilson, N., Slaney, D., Baker, M.G., Hales, S. & Britton, E. (2011). Climate change and infectious diseases in New Zealand: a brief review and tentative research agenda. *Reviews on Environmental Health* **26**: 93-99.

Wu, P.C., Guo, H.R., Lung, S.C., Lin, C.Y. & Su, H.J. (2007). Weather as an effective predictor for occurrence of dengue fever in Taiwan. *Acta Tropica* **103**: 50-57.