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Short communication: **Impact of climate variability on the incidence of dengue in Mexico**

M. Hurtado-Díaz[1], H. Riojas-Rodríguez[1], S. J. Rothenberg[1,2], H. Gomez-Dantés[3] and E. Cifuentes[1]

1 *National Institute of Public Health, Cuernavaca, Morelos, Mexico*
2 *CINVESTAV-IPN, Merida, Yucatán, Mexico*
3 *Mexican Social Security Institute, Mexico City, Mexico*

Summary We evaluated the impact of weather variables and climatic indicators associated with the incidence of dengue in two municipalities of the state of Veracruz, Mexico, from 1995 to 2003. A retrospective ecological study was conducted, using time-series analysis in which we compiled the weekly reported cases of dengue and the weather and climatic parameters: temperature, rainfall and sea-surface temperature (SST), the latter as an El Niño Southern Oscillation indicator. We statistically evaluated the data with autogressive models. The models' predictive abilities were evaluated using data collected from 1995 to 2002 and were validated with those observed for 2003. Each degree Centigrade increase in SST was followed by an increase in the number of dengue cases: 46% in San Andrés Tuxtla ($P = 0.001$) 16 weeks later and 42% in Veracruz 20 weeks later ($P = 0.002$). Increases in weekly minimum temperature and rainfall were also significant factors in the increase in the reported cases of dengue. We recommend future studies using the same method, involving larger populations with different geographic location, climate and weather. We also recommend strengthening environmental, health and entomological surveillance systems to improve preparedness and emergency responses.

keywords El Niño Southern Oscillation, El Niño, climate variability, weather, dengue, vector-borne diseases, time series

Introduction

Dengue is one of the most relevant public health diseases in developing countries (Guzmán & Kourí 2002). It occurs in more than 100 countries and an estimated 2.5 billion people are at risk of infection (WHO 2000). Each year, 50 to 100 million infections occur worldwide and in Latin America; the number of cases increased from 236 000 in 1995 to more than 1 000 000 in 2002 [Pan American Health Organization (PAHO) 2004].

Dengue's main vector is the *Aedes aegypti* mosquito (Ibañez-Bernal & Gómez-Dantés 1995), which had been eradicated in Mexico in the 1960s. Clinically, dengue has been recognized in Mexico since 1941, and since 1981, all the four serotypes have been identified across the country. The largest national epidemic was registered in 1997, with 53 000 cases of classic dengue, 980 cases of haemorrhagic dengue and 37 deaths (PAHO 2001). But environmental and epidemiological conditions for dengue outbreaks vary nationwide. Larvae breeding sites may be a result of socio-cultural factors, some of which may interact with seasonal variables and water scarcity-related behaviour. Substandard housing, water storage practices and lack of garbage collection facilities may increase health risk (Lozano *et al.* 2002; Cifuentes *et al.* 2006). Environmental factors, such as temperature, humidity, precipitation and altitude determine dengue's transmission (Gómez-Dantés *et al.* 1995).

From 1988 to 2002, Veracruz was one of the states with the highest number of infections, with 14.6% reported in Mexico during this period and an average rate of 27.9 cases per 100 000 inhabitants (SSA 2003b). In 2003, there were 6996 cases of dengue reported in Mexico, and Veracruz again reported a higher incidence of classic dengue, with a rate of 14.95 per 100 000 inhabitants (SSA 2003a). Veracruz has a very diverse climate. Nearby mountain ranges modify the tropical characteristics governed by its geographical location. Two meteorological phenomena influence the climate of this state: cyclones that occur after the rainy season (autumn) and extend the rains; and the cold fronts or 'northern winds', frequent in winter and sometimes lasting until spring.

El Niño Southern Oscillation (ENSO) is an anomalous condition in ocean temperature in the eastern tropical Pacific Ocean (Magaña 1999) in which warm events (known as 'El Niño') and cold events ('La Niña') take place (Trenberth 1997). Meteorological evidence suggests that the warm phase of ENSO influences the variability of the climate in Veracruz (Magaña 1999). The warm phase of ENSO occurs when the sea-surface temperature (SST) exceeds the mean 1950–1979 period temperature by 0.4 °C for at least six consecutive months in Niño 3.4 Region. This happens every few years, changing the local and regional ecology, both of which may experience extreme climatic events (heavy rain, floods, heat).

El Niño Southern Oscillation seems to influence the generation, intensification and redistribution of a number of vector-borne diseases (Nicholls 1993; Patz *et al.* 1996; Epstein *et al.* 1998; Kovats 2000) and increases the risk of dengue outbreaks in certain geographical regions with limited disease control (Reiter 1998), where meteorological conditions are associated with the ENSO cycle (Hales *et al.* 1996, 2002; Seghal 1997; Gagnon *et al.* 2000).

The links between ENSO climate and dengue however have not been clearly established. We tested the hypothesis that the ENSO cycle affects the weekly incidence of dengue cases in municipalities of Veracruz, Mexico, adjusting for local weather.

Materials and methods

We conducted an ecological study with retrospective time-series analysis (Loomis *et al.* 1996; Checkley *et al.* 2000; Tong and Hu 2001) using dengue cases recorded each week in the municipalities of San Andrés Tuxtla and Veracruz from 1995 to 2003 (Figure 1). Reported dengue cases, serotypes of dengue present in the state and monthly *A. aegypti* Control Program activities (larvicide application, spatial spraying, physical control and entomological verification) were obtained from the Veracruz State Health Ministry. Daily weather data on precipitation and maximum and minimum temperatures were obtained from meteorological stations located in the state of Veracruz, operated by the National Meteorological Service and Regional Gulf-Central Administration. Census data from

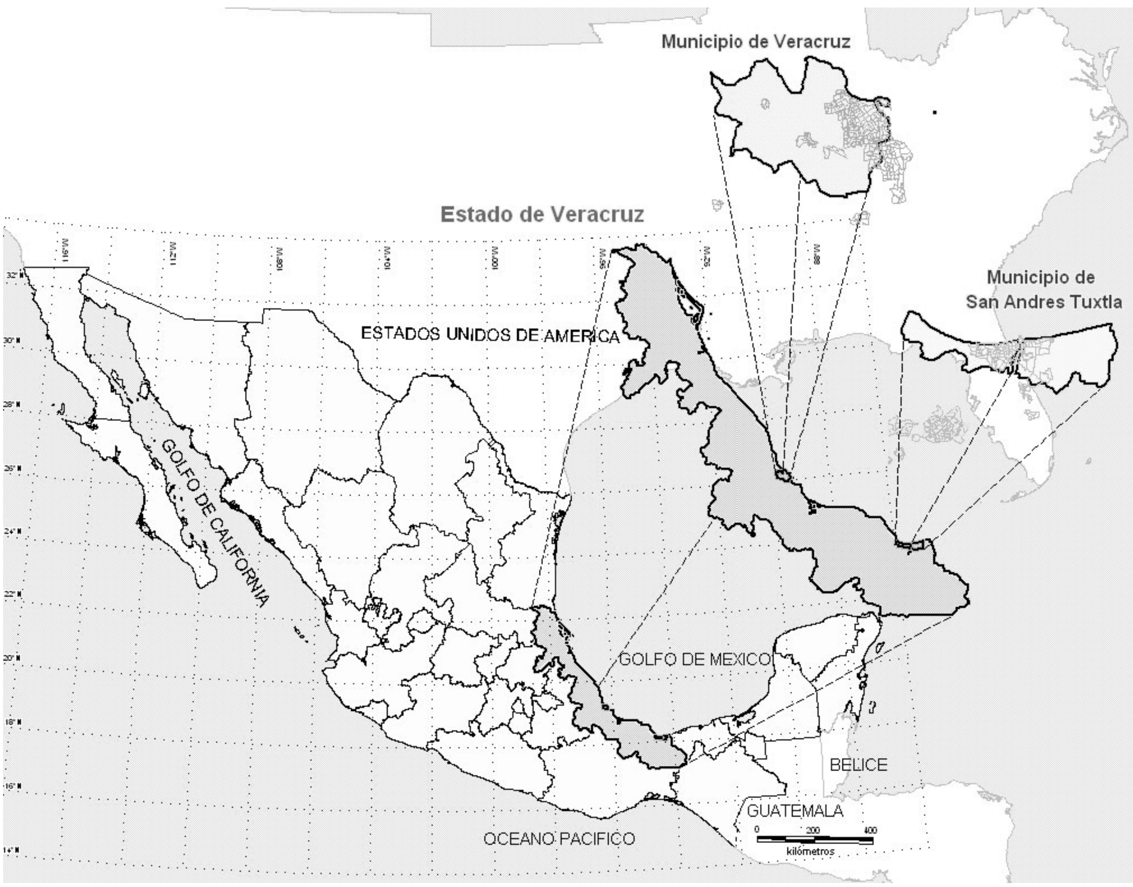

Figure 1 Location of study zone.

1990 to 2005 for the municipalities of Veracruz and San Andrés Tuxtla were obtained from the National Institute of Statistics, Geography and Informatics of Mexico (INEGI 1992, 1996, 2001, 2006).

A geographical information system (MapInfo Corporation, 2005) allowed us to select the most representative meteorological station in the studied municipalities in terms of geographical location, altitude, temperature and precipitation, using digital cartography (including contour curves, isotherms and isohyets). We located the coordinates of the stations that registered daily data in the state of Veracruz for the entire study period. As these data were not recorded automatically, validation was done by comparing the time-series daily value and the magnitude of the climate variable with the time-adjacent values of the same station and same day values of adjacent stations, to detect out-of-range differences. Maximum and minimum weekly temperatures and accumulated weekly precipitation were calculated. As an ENSO indicator, we used weekly records of SST obtained from a specific zone of the Pacific Ocean [Niño 3.4 region (5S-5N; 170W–120W)] [International Research Institute for Climate Prediction (IRI) 2004]. These data were downloaded from the United States National Ocean Atmospheric Administration (NOAA 2004).

We examined temporal trends and seasonal variations of dengue cases by week, maximum temperature, minimum temperature, precipitation and *A. aegypti* Control Program activities. To establish an association between the number of cases of dengue and SST, maximum temperature, minimum temperature and precipitation, we calculated cross-correlation coefficients between autoregressed dengue series and each of the independent variables, with different lag times. The range of lag times examined was based on literature reports and the plausibility that climate and weather variables influence dengue transmission.

The four data points of human population variation for each municipality completely encompassed the date ranges of the dengue time series. We fitted a second-order polynomial regression to characterize the non-linear increase in population of each municipality over the 15-year period, and derived weekly predicted values of population from the regressions throughout the date range of the dengue time series.

Time series usually display serial correlation (autocorrelation), violating one of the assumptions of ordinary least square regression models that observations of the dependent variable be independent of one another. In time series, consecutive values are correlated. Efficient and unbiased estimation depends on the knowledge of such correlation structure (Uriel 1992). We first determined that the two dengue time series were stationary, and then empirically determined the optimum autoregressive lag adjustment for the dengue series in each municipality to satisfy the requirements of Bartlett's periodogram-based white noise test (Bartlett 1955; Newton 1996) and the Pormanteau test for white noise (Box & Pierce 1970; Ljung & Box 1978). The residuals of the 'whitened' autoregressed series were evaluated for normality. Finding that residual distributions were skewed towards higher values, we added one case to each weekly case count and natural log transformed the adjusted weekly case counts. We repeated the empirical autoregressive adjustments and examined the resulting residuals for lack of serial correlation. The resulting residuals approximated a normal distribution.

The optimal time lag for the independent weather and climate variables was determined by cross-correlating the independent series against the auto-regressed dengue series. We operated within lag constraints that were biologically and physically plausible for the dengue–climate–weather system under study and selected the time lag producing the highest cross-correlation within those constraints. The predicted population size weekly series was added to each model to adjust dengue cases for changes in population over the period.

Adequacy of final models was evaluated with normality, heteroskedasticity and white noise tests on the residuals. We compared the coefficients of the independent variables in the two municipalities to verify the relative effect size between the two municipalities studied. Finally, we evaluated the predictive value of each model using the data collected from 1995 to 2002 and then validated the prediction of dengue from the model with dengue cases observed for 2003. We compared the mean square error measurements of the 2003 model year using the predicted values from the 1995 to 2002 model with the predicted values from the model evaluated with all years, 1995 to 2003. Statistical calculations were done using Stata 9.2 (Stata Corporation, San Antonio, TX, USA).

Results

From 1995 to 2003, there were 37 005 cases of dengue reported in the state of Veracruz; 6.8% occurred in San Andrés Tuxtla and 12.2% in Veracruz. Dengue rates were highest in both municipalities in 1996–1997 and 2002. All four dengue serotypes have been identified in the state since 1995.

From 1995 to 2003, San Andrés Tuxtla had a greater mean annual precipitation (1900 mm *vs*. 1549 mm), and a lower mean annual minimum temperature (15.9 °C) than Veracruz (18.1 °C). The months of July, August and September were rainier, and along with May and June, hottest (Figure 2). The highest SST was recorded during the periods 1997–1998 and 2002–2003, coinciding with the highest rates of dengue of years 1997 and 2002 in both municipalities (Figure 3). The maximum cross-correlations of precipitation, minimum temperature and SST, respectively, with the auto-regressed dengue series were 0.119, 0.119 and 0.084 in San Andrés and 0.225, 0.099 and 0.092 in Veracruz.

In San Andrés Tuxtla, adjusted auto-regressive models (Table 1) showed that the weekly number of dengue cases – with a lag of 16 weeks – increased by 46% for every increase of 1 °C of SST; by 3.8% for every increase of 1 °C in minimum temperature during the same week; and by 1.3% for every increase of 1 cm of precipitation with a lag of 2 weeks. In Veracruz, the number of dengue cases – with a lag of 20 weeks – increased by 42% for every 1 °C increase in SST; by 4.8% for every 1 °C increase in minimum temperature the same week; and by 2.1% increase of cases for every 1 cm of precipitation with a lag of 3 weeks. We found no significant difference of weather and climate variable coefficients between the two municipalities (Table 2). This suggests that the effects of the climate and weather variables included in the models on dengue were the same for San Andrés Tuxtla and Veracruz during 1995 to 2003.

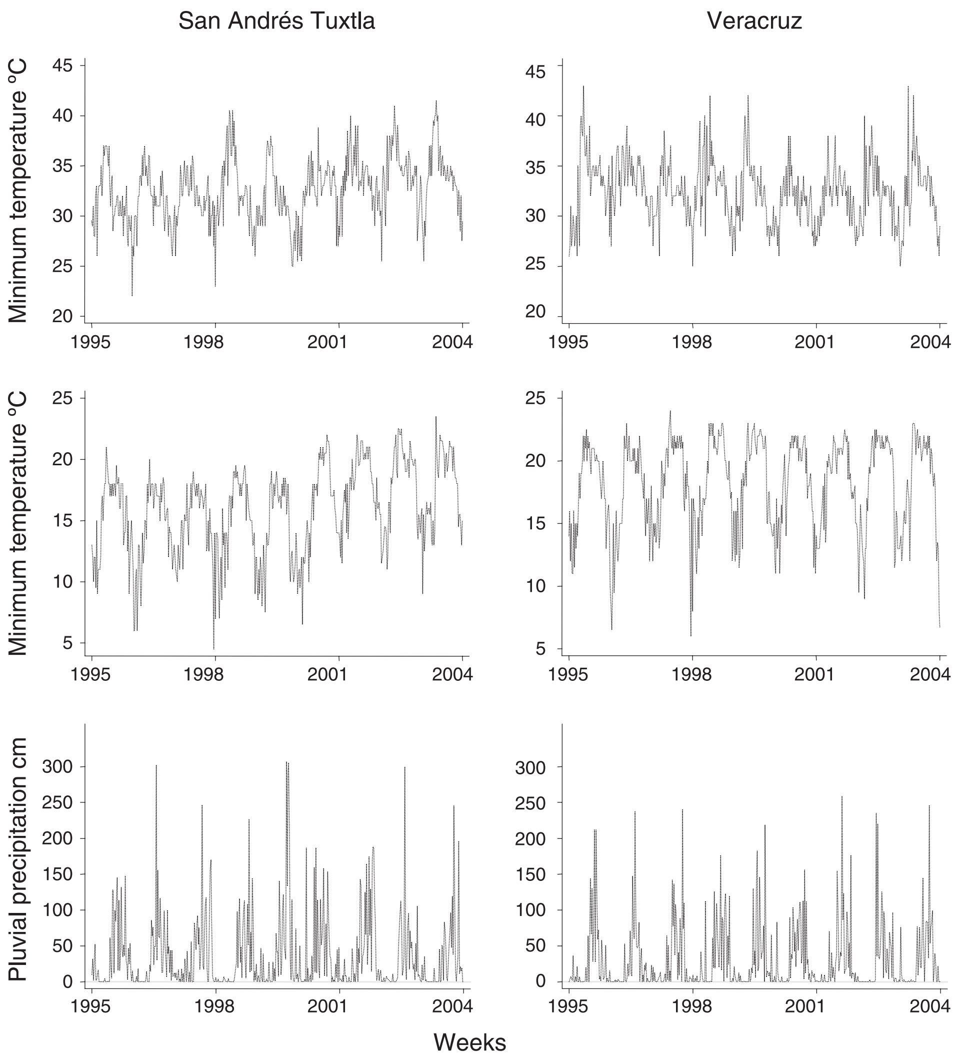

Figure 2 Weekly variation of maximum temperature, minimum temperature and precipitation at San Andrés Tuxtla and Veracruz municipalities during the period 1995 to 2003.

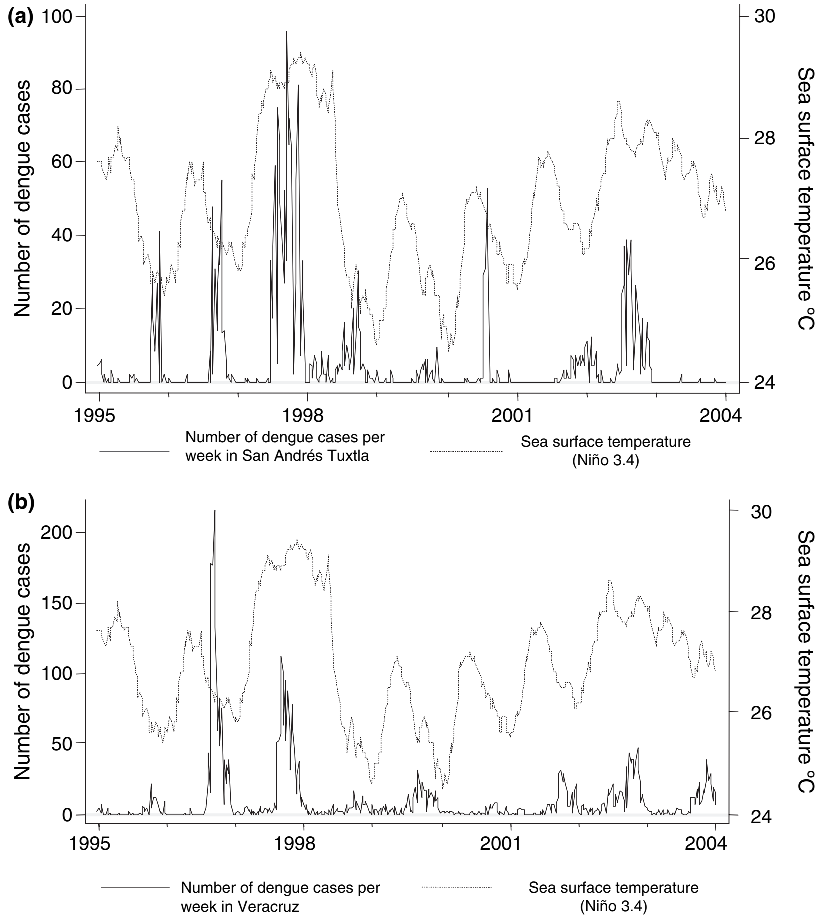

Figure 3 Weekly records of sea surface temperature and number of dengue cases in (a) San Andrés Tuxtla municipality and (b) Veracruz municipality, during the period 1995 to 2003. Note the difference of scale in the number of weekly dengue cases in the two municipalities.

Table 1 Adjusted coefficients between natural logarithm of weekly cases of dengue [ln (# cases+1)], climate, weather and population variables. San Andrés Tuxtla and Veracruz municipalities, 1995–2003

Climate variable	San Andrés Tuxtla β 95% CI	Veracruz β 95% CI
Minimum temperature (°C)	0.044 (0.003, 0.084)	0.058 (0.018, 0.098)
Precipitation (cm)*	0.022 (0.001, 0.038)	0.022 (0.008, 0.037)
Sea surface temperature (°C)†	0.510 (0.247, 0.774)	0.453 (0.184, 0.723)
Population‡	0.179 (−0.963, 1.321)	0.110 (−0.072, 0.292)
Constant	−16.08 (−34.10, 1.95)	−16.93 (−28.809, −5.068)
AR(1)§	0.450 (0.373, 0.528)	0.397 (0.303, 0.490)
AR(2)§	0.226 (0.147, 0.305)	0.341 (0.247, 0.435)
AR(3)§	0.087 (0.006, 0.169)	0.083 (−0.012, 0.178)

CI, confidence interval.
*Lags of 2 and 3 weeks for San Andrés Tuxtla and Veracruz, respectively.
†Lags of 16 and 20 weeks for San Andrés Tuxtla and Veracruz, respectively.
‡Rate per 10 000 inhabitants.
§AR(*n*) Autoregressive terms with a lag of *n* weeks.

The effect of population growth on dengue cases was positive, but statistically not significant. To evaluate the predictive ability of the models, we used the model calculated with only data from 1995 to 2002 to predict cases in 2003 (out of model predictions) based only on calculated population and observed climate and weather variables during that year. In prediction charts (Figure 4), we found a good fit of predicted values with observed

Table 2 Difference of modelled climate and weather variable effects in San Andrés Tuxtla and Veracruz municipalities, 1995–2003

Climate variable	β 95% CI
Minimum temperature (°C)	−0.102 (−0.045, 0.024)
Precipitation (cm)	−0.001 (−0.002, 0.001)
Sea surface temperature (°C)	0.035 (−0.227, 0.297)

CI, confidence interval.

values; the number of predicted weekly dengue cases were underestimated, but followed the same pattern. The mean square error values were 0.179 for the predicted year 2003 and 0.099 for the modelled year 2003 in San Andrés and 0.447 and 0.428 for Veracruz. Smaller values reflect better correspondence of the model with the data. No predictive association between increase in *A. aegypti* control activities and changes in dengue incidence patterns was detected and this variable was not included in the models.

Discussion

This study shows that an increase in SST, minimum temperature and precipitation is associated with an increase of dengue transmission cycles in the coastal municipalities of the Gulf of Mexico. As far as we know, this is the first study to report an association between an ENSO indicator and dengue incidence in Mexico.

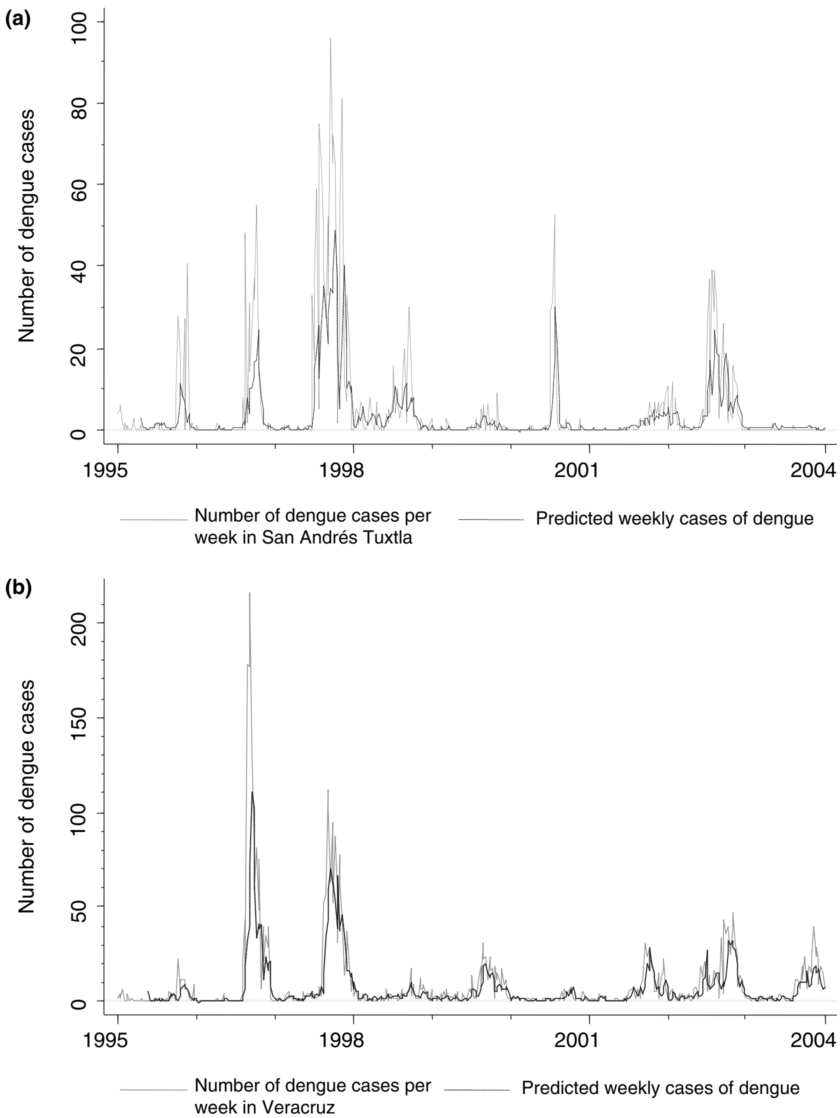

Figure 4 Weekly records of the number of dengue cases and prediction of the number of weekly cases of dengue in (a) San Andrés Tuxtla municipality and (b) Veracruz municipality for the period 1995 to 2003. Note the difference of scale in the number of weekly dengue cases in the two municipalities.

In the last two decades, there has been an intense debate about the connection between climate variables and the emergence and transmission of vector-borne diseases. The roles of temperature and precipitation are well documented (Gould *et al.* 1970; Foo *et al.* 1985; Watts *et al.* 1987; Halstead 1997; Kuno 1997; Rodhain & Rosen 1997; Gubler 1998; Koopman *et al.* 1999, Reiter 1999). The most likely mechanisms involve weather extreme events and multiplication of mosquito-breeding sites (resulting from collapse of water supplies and sanitation services) on the one hand, and a shorter extrinsic incubation period (EIP) of the virus inside the mosquito on the other hand.

In Barbados, from 1995 to 2000, the correlation between weekly dengue cases and minimum temperature was strongest at a lag of 12 weeks and with the maximum temperature at a lag of 16 weeks; for precipitation, a weaker correlation occurred at a lag of 7 weeks (Depradine & Lovell 2004). In contrast, we found weekly effects on dengue cases by precipitation at a lag of 2 and 3 weeks, suggesting that precipitation is a useful predictor. Despite the fact that the main habitats of *A. aegypti* larvae are water containers, our findings help understand why peak dengue transmission occurs in the hot rainy months.

El Niño Southern Oscillation is the most important climate cycle contributing to inter-annual climate variability (Enfield & Nuñez-Mesta 1999). However, the intensity of the climate anomalies occurring in each ENSO event varies. Vector-borne diseases, such as dengue show great yearly variations that may be partly explained by meteorological factors. Studies focussed on analysing ENSO effects on dengue have reported different results, showing that local climate changes associated with ENSO are important to model the impact of climate variability on dengue cases.

Gagnon *et al.* (2001) associated the increase in dengue cases with mean temperature and precipitation influenced by El Niño. Greater risk for dengue epidemics have been found during the warming phase of ENSO (El Niño years) in Colombia and Indonesia, and in the year following this event, in French Guiana and Suriname. Our study differs in that we used a continuous variable (SST) associated with climate variability instead of the dichotomous variable of El Niño years. The use of El Niño years (Poveda *et al.* 2001) as a time variable is imprecise because this phenomenon is used as an indicator variable each year an El Niño event is registered. An El Niño event may start in 1 year and end in the next but its effect on distant climate may be limited to just one of those years (Kovats *et al.* 2003).

Although previous studies have found an association between dengue and ENSO using an indicator variable to measure this anomaly, these studies used monthly national aggregated data (Giraldo *et al.* 1999; Hales *et al.* 1999; Rifakis *et al.* 2005). On five islands of the South Pacific, between 1970 and 1995, the monthly reports of dengue cases were positively correlated with the ENSO parameter Southern Oscillation Index and local temperature and precipitation values (Hales *et al.* 1999). Rifakis *et al.* analysed the relationship between the cases of dengue and climate variables, such as minimum and maximum temperatures and precipitation in Venezuela, using, as did Hales *et al.*, monthly units of analysis. Our effort differs from these studies in that we aggregated these data weekly, making associations within a shorter lapse of time, which is biologically plausible with the timing of the mosquito life cycle (Watts *et al.* 1987).

Different models have been used to assess the relationship between climate and weather variability and dengue. Hopp & Foley (2001) examined the global-scale relationships between weather variables (precipitation, temperature, relative humidity and solar radiation), *A. aegypti* populations, and cases of dengue using a numerical model of mosquito population dynamics. They found that variations in climate can induce variations in *A. aegypti* populations and these climate-induced variations are strongly correlated with the reported dengue cases. Hales *et al.* (2002) have elaborated global dengue distribution maps based on the development of models that include climate factors. But this method does not produce a greater understanding of the forces that drive annual changes in the incidence of this infectious disease (Kovats *et al.* 2003). A recent study between 1986 and 1992 in Thailand shows a strong association between monthly dengue cases and ENSO, using wavelet approaches (Cazelles *et al.* 2005). Though these results are consistent with our findings, we used auto-regressive models enabling us to assess how many of the past weekly values of dengue and climate and weather variables contribute to predict dengue cases in the municipalities we studied.

Our study contributes to the understanding of the ENSO–climate–dengue relationship by analysing small geographic areas (municipalities), aggregating weekly data of temperature and precipitation variables as the main conductors of the biological process by which climate and weather variability affects health (Kovats *et al.* 2003). We used SST as an indicator of climate variability to quantify the impact of temporally and spatially distant climate signals on the Gulf of Mexico, where warm ENSO events reduce the number of hurricanes and tropical storms from June to November. On the contrary, cold events are characterized by more hurricanes and tropical storms during this same period (Magaña 1999). However, the amplitude of the ENSO signal in this region shows a systematic lag of one to two seasons (3–6 months) against the temperature of the equatorial Pacific. This may explain the lag of 16–20 weeks between the SST change and the increase in dengue.

It is important to emphasize that although the effects of ENSO warming in the Pacific are followed by much smaller changes in the Gulf of Mexico, this does not mean that ENSO warming has no effect on the Gulf's climate; ENSO may affect other variables in the global ocean and atmospheric system (i.e. precipitation, tropical storm activities) (Cavazos 1999; Enfield & Nuñez-Mesta 1999).

Climatic factors affect dengue transmission depending on the geographical area (Ibañez-Bernal 1987; Herrera-Basto *et al.* 1988; Ibañez-Bernal & Gómez-Dantés 1995). We found no significant differences of climate variability effects influenced by SST in the two municipalities studied, although having different orography, hydrography, altitude and type of climate, they are influenced equally by the same signal of this event in the Gulf of Mexico.

We also thought that factors other than climate indicators and weather might confuse the ENSO–climate–dengue association; hence, we considered them when developing our models. These, however, were not included for a number of reasons. First, our study had demographic limitations inherent to working with few municipalities. We were unable to assess the effects of social vulnerability as measured by the margination index, nor the effects of population density or the immigration/emigration ratio because migration data were not reported at weekly intervals. Second, *A. aegypti* control programmes (larvicide application, spatial spraying, physical control and entomological verification) do not predict dengue case variability in time. Our initial hypothesis was that the number of dengue cases would be reduced during the period of intense *A. aegypti* control programme activities. On the contrary, we found that these control activities only increased after the rise of dengue cases.

Another important factor predisposing to outbreaks is a change in dengue immunity. However, there was no weekly or monthly immunity information available for each of the circulating serotypes by municipality, as our study demanded, for these available data were aggregated by sanitary district and by year, not by municipality and by week. From 1995 onwards, all the four serotypes started to circulate in the state of Veracruz. This coincides with the initial period of our study; hence, with regards to the time series we analysed, the association was not modified by the introduction of new serotypes and we did not include them in the models.

Time-series analysis is inherently empirically driven. Adjustment of the optimal auto-regressive lag structure depends on the auto-correlation characteristics of the dependent variable. The goal of this adjustment is to take out serial dependence in the dengue series, leaving the resultant residuals amenable to ordinary least square analysis. Similarly, the selection of the optimum lag time used for the independent variables was discovered by multiple testing, though we operated within time lag constraints set by biological and physical plausibility. Thus, while temperature and rain effects could plausibly affect mosquito activity cycles, the growth and development of the mosquito vector, and larval habitat for only a period of a month around the events measured, SST could conceivably lag dengue cases by up to two seasons owing to its known time-lagged effect on climate. The specific auto-regressive lag structure and the lag length of the weather and climate variables found here are likely linked to the locations studied. The specific lag lengths may be proxies for variables not explicitly measured. They could vary in the same locations over periods of time much longer than the period studied here or across widely different locations, where these supposed unmeasured variables change. It should also be emphasized that much of the predictive power of auto-regressive time series models is derived from the auto-regressive terms themselves, notwithstanding the statistically significant effects of the SST and weather variables.

Nonetheless, we find it significant that an index of ENSO, the SST, independently predicts dengue cases 4–5 months ahead of time, even controlling for local temperature and precipitation, two of the weather variables most affected by ENSO.

Although studies carried out with other vector-borne diseases, such as malaria, have not found evidence to support that change in population immunity may explain epidemics that last longer than 3 to 5 years (Hay *et al.* 2000), we tried to take into account the proportion of susceptible persons within a population (to specific serotype, not cross immunity) because it is a determining factor in the incidence of dengue cases. Population growth from one year to the next was estimated in the models to control for this possible source of secular dengue increase, but we found no statistically significant associations between the increase of dengue cases and the growth of the population.

Although obtaining climate variable data from only one meteorology station may produce errors if data are not representative of the studied zone (Malhi & Wright 2004), we believe this was not a problem in our study because we selected the most representative station of the studied municipalities in terms of geographic location, altitude, temperature and precipitation.

The recorded dengue cases used in our study followed standard procedures during the study period. The available information did not permit us to determine whether the reported dengue cases represented the total number of cases acquired in the municipalities of our study or if a percentage of them were acquired in another place. However, in the state of Veracruz, between 1995 and 2000, 1.3% of the population >5 years of age of the state of Veracruz emigrated, while 0.5% immigrated (INEGI 2001). The majority of the immigrant population comes from non-endemic states, such as the State of Mexico (22.96%) and the Federal District (17.70%). Therefore, there is little reason to assume that this factor resulted in a significant bias during the period of our study.

Under-estimation of dengue cases in the calculated predictions is a consequence of the variables affecting transmission that were not included in the model; it is also attributed to the fact that predictive models tend to under-estimate the number of cases.

Conclusions

The results proposed in this study satisfactorily model the pattern of dengue cases in two municipalities of the state of Veracruz. Considering that climate integrates the factors that define seasonal transmission and establishes if dengue cases are endemic, epidemic or outbreaks (Gómez-Dantés *et al.* 1995), these results may be useful in the development of early warning system (EWS) based on climatic elements for prevention and control of dengue epidemics in the municipalities of Veracruz studied, as proposed by WHO (2004).

Climatic forces may work in parallel with socio-cultural and epidemiological conditions. Larvae breeding sites may be a result of poor housing, water scarcity-related behaviour, in addition to the lack of garbage collection facilities and weak health institutions, all of which create the broth supporting the re-emergence of dengue and other global calamities (Garret 1994; Cifuentes *et al.* 2006).

This EWS should be complemented with other variables that influence the transmission of the disease, such as weekly reports of detected serotypes. Further studies are needed to validate an EWS that incorporates the factors that affect dengue transmission. Notably, its sustainability will largely depend on the ability of the meteorology centres to improve climate predictions. Thus, we recommend future studies using similar methods of more municipalities with different geographical location and climate.

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Corresponding Author H. Riojas-Rodríguez, National Institute of Public Health, Av. Universidad No. 655, Col. Sta. María Ahuacatitlán, Cuernavaca, Morelos C.P. 62508, México. Tel.: +777 3293 060; Fax: +777101 2937; E-mail: hriojas@correo.insp.mx