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Associations between Dengue Hospitalizations and Climate in Can Tho, Vietnam, 2001-2011

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Abstract

In Vietnam, dengue fever is a major cause of hospitalization with over one million cases reported between 1991 and 2004. Changes in the incidence of dengue in Can Tho city due to increased temperature and changes in precipitation, are anticipated. In an effort to better characterize the relationship between climate and dengue, we examine the associations between weather variables and dengue hospitalizations in Can Tho between 2001 and 2011. Monthly data on hospitalized dengue cases and means of temperature, rainfall and humidity were recorded from 2001 to 2011. We used the Box-Jenkins approach to modelling of time series to assess the association between these factors. This model was validated by the Portmanteau test. Our results revealed that the highest dengue incidences in Can Tho occur between July and December. After adjusting for seasonality, the rate of dengue hospitalizations was significantly associated with relative humidity with a lag of one month. Rainfall and temperature were not predictors of dengue hospitalization rate. In conclusion, these data suggest that maximum relative humidity (with a one month lag) is an important determinant of dengue hospitalizations. Enhanced vector control during months with high humidity may be an important approach to prevent dengue transmission.

Keywords: dengue fever; incidence; climate; hospitalizations; ARIMA model

1. Introduction

Infection with one of four dengue virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4; family *Flaviviridae*; genus *Flavivirus*) causes an acute febrile syndrome called Dengue Fever. Mosquitoes of the genus *Aedes* (*Ae. Aegypti*, and to a lesser extent, *Ae. albopictus*) are its vector. It is estimated that 390 million people worldwide are infected yearly with 96 million manifesting symptoms (Bhatt *et al*., 2013). Approximately one percent of the dengue cases are complicated by hemorrhage, hemodynamic instability, and/or end-organ damage (Rigau-Pérez, 2006). In endemic regions in Asia and Latin America, severe dengue is a leading cause of morbidity and mortality. At present, there are no approved specific therapies (Schwartz *et al*., 2015). A vaccine has been very recently developed and registered for use in endemic regions (WHO, 2016), but vector control remains critical for disease prevention.

In Vietnam, dengue fever is an important public health issue and a leading cause of illness and death (WHO, 2011). In 2010, over one hundred thousand cases of dengue were reported (Central Institute for Hygiene and Epidemiology, 2010). It is estimated that one third of the cost of dengue management is assumed by the government, and the remainder is covered by the patients themselves (Can Tho Department of Health, 2011). This cost does not include the number of working days lost by patients and caregivers.

The burden of disease in Vietnam is greatest in the Mekong Delta (Vu *et al*., 2014). In the city-province of Can Tho, which lies in the heart of the delta, the annual dengue hospitalization rate has been approximately one in one thousand per year (Center for Preventive Medicine of Can Tho City, 2009; 2010; 2011). Many studies have examined the relationship between climate and dengue incidence (Thai and Anders, 2011; Thai *et al*., 2010; Gharbi *et al*., 2011; Descloux *et al*., 2012; Banu *et al*., 2011), but it has been difficult to generalize the findings due to regional variability and heterogeneity of methods used. In Vietnam, Thai *et al*. (2010) examined climate and dengue incidence in Binh Thuan Province in the middle of Vietnam using wavelet analysis, and found a positive association between dengue incidence and precipitation, temperature, and humidity, and identified a periodic multi-annual cycle. Pham *et al.* (2011) analysed dengue incidence, larval indices, and weather variables in Vietnam's central highlands, and also found that precipitation, temperature, and humidity were positively associated with the risk of dengue. However, in examining multiple provinces in Vietnam, Vu *et al.* (2014) found that while temperature, precipitation and humidity were significantly associated with dengue in most of the provinces, the direction and degree of association varied greatly.

Thus, in order to understand the influence of weather variables on dengue transmission in Can Tho, inferences cannot be made reliably from the literature alone. We therefore conducted a time series analysis of the dengue hospitalization rate and weather variables in Can Tho between 2004 and 2011. The aim of this work is to lay the groundwork for the adaptation of dengue prevention and control strategies to a changing climate.

2. Materials and Methods

2.1. Study site

Can Tho city is one of five major cities in Vietnam. It lies in the heart of the Mekong Delta and has a population of 1.2 million (Can Tho City Statistics Department, 2012). The city limits include rural areas in which 65% of the population resides. With a population density of 852 people/km^2, the city is considerably denser than the country wide average for Vietnam (289 people/ km^2). Can Tho has a tropical monsoon climate, with a rainy season from May to October, and a dry season from November to April. Average humidity is 83% and annual rainfall is between 1,500 to 1,800 mm/year. The city has been experiencing increasing flooding with parts of the city inundated for two months per year, (Can Tho Climate Change Office, 2012). The mean annual temperature is 27°C, but a rise of 0.4°C has been recorded since 1960 (World Bank, 2015).

2.2.Dengue hospitalizations

Dengue hospitalizations have been recorded between 2001 and 2011 but reliability is an issue prior to 2004. The monthly rate of hospitalization was calculated based on clinically defined cases in accordance with WHO diagnostic criteria (WHO, 2009). Data gathered included name, age, sex, address, hospital admission date, diagnosis, and disease severity.

2.3.Meteorological data

Meteorological data collected included monthly averages, minimums, and maximums for rainfall, temperature, and humidity from the Can Tho meteorological and hydrological station, located in the center of Can Tho city.

2.4. Autoregressive integrative moving average (ARIMA) models

Autoregressive integrative moving average (ARIMA) models have proven very useful for the analysis of time-series data, explicitly accounting for temporal dependence between observations (Helfenstein, 1996). We employed the Box-Jenkins approach to modelling dengue hospitalization rates in Can Tho, in which we: 1) examined the observations for stationarity (constant mean and variance over time); 2) analyzed the data for seasonal variance; 3) specified the model by inspecting its autocorrelation structure; 4) estimated model parameters; and 5) refined the model and examined its goodness-of-fit. The monthly auto-correlation function (ACF) and the partial auto-correlation function (PACF) were examined to determine the lag. Residuals of the model were checked for white noise with Bartlett's Portmanteau test. Statistical analysis was conducted in STATA v11.0 (Statacorp, College Station, TX).

3. Results and Discussions

3.1.Dengue hospitalization rate

There were significant year-to-year variations, with peak rates occurring in 2004. Dengue hospitalization rates declined in subsequent years, from 2.2/1000 in 2004 to 1.3/1000 in 2007, then 0.8/1000 in 2010, and 0.6/1000 in 2011.The annual incidence of new dengue cases remained high. (Fig. 1(a)).

A clear seasonal trend was observed. Mean monthly hospitalization rates during the months of July through December were approximately twice that encountered in the period between January and June. Rates were consistently lowest during the month of February (Fig. 2(b)).

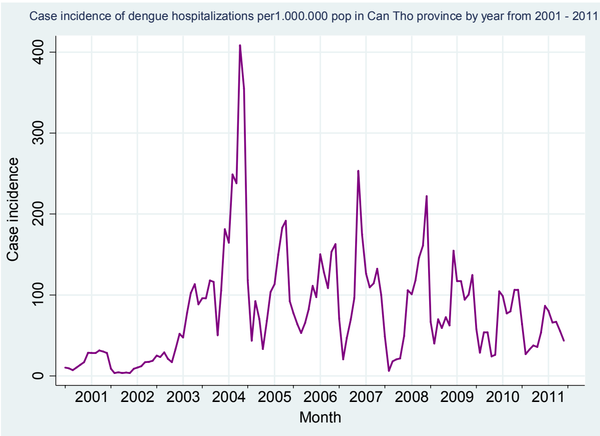
3.2. Seasonal variation

3.2.1. Temperature

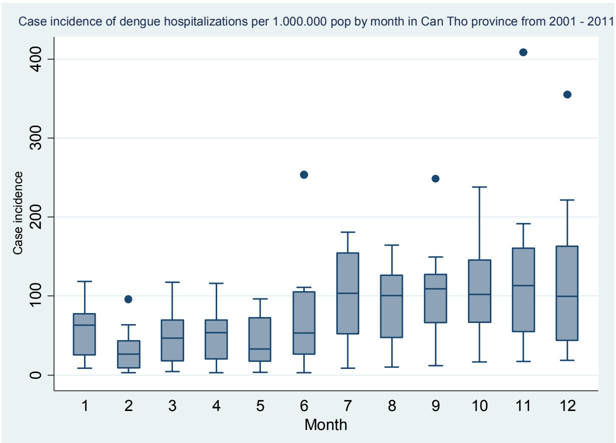
Average monthly temperatures from 2001 to 2011 were plotted to place the dengue hospitalization data in a larger climate context. Fig. 2(a) depicts monthly average temperatures. Maximum temperatures ranged between 21.1°C and 34.9°C (mean 27.1±1.0°C, 95% CI 26.9 - 27.3°C), with hottest periods occurring in April (Fig. 2(b)). Minimum temperatures fluctuated between 21.1°C and 26.9°C (mean 24.3±0.9°C, 95% CI 24.1 - 24.5°C) (Fig. 2(c)).Temperature is an important factor in the rate of mosquito development, biting behaviour, and the dengue virus extrinsic cycle, with both elements slowing down significantly below 20°C (Watts *et al*.,1987).

3.2.2. Precipitation

This peaked in October with an average rainfall of 265.3±25.8mm (95% CI, range from 210.5 to 320.1mm). Lowest precipitation occurred in February (mean 6.2±3.4mm, 95% CI range from -1.1 to 13.4) (Fig. 2(d)). Precipitation is clearly important for the formation of breeding sites, but excessive precipitation may washout breeding sites. In addition, key breeding containers may be large capacity (>50L) water storage containers that are less influenced by day-to-day rainfall (Kay and Nam, 2005)

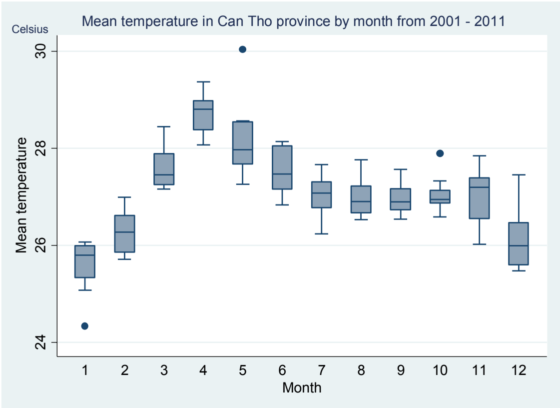


(a) incidence by year

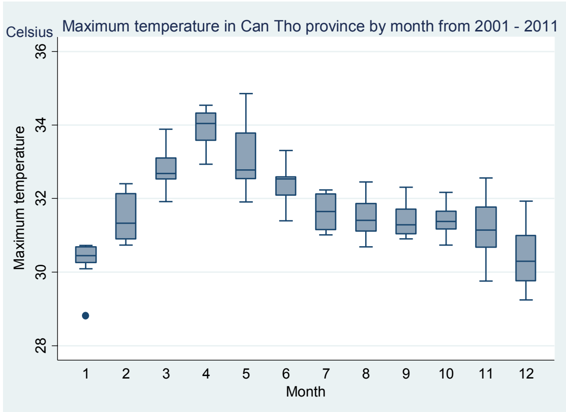


(b) incidence by month

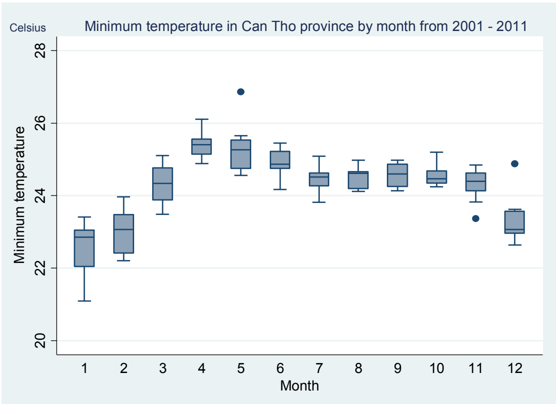
Figure 1. Dengue hospitalization incidence per 1,000,000 population by year, Can Tho City (2001-2011)
(a) Incidence by year; (b) incidence by month: 12 bars symbolize to the case incidence of dengue hospitalization in 12 months. In each bar, the horizontal lines represent (from the top) the maximum, the third quartile, the median, the first quartile and the minimum of case incidence. The shaded box represents the middle 50% of the distribution (between the first and third quartiles). Five dots symbolize to five above outlier values.



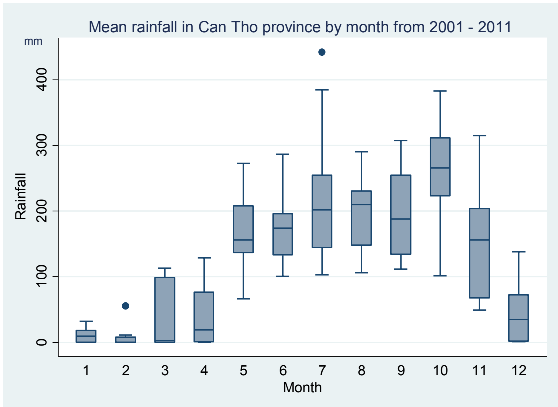
(a)



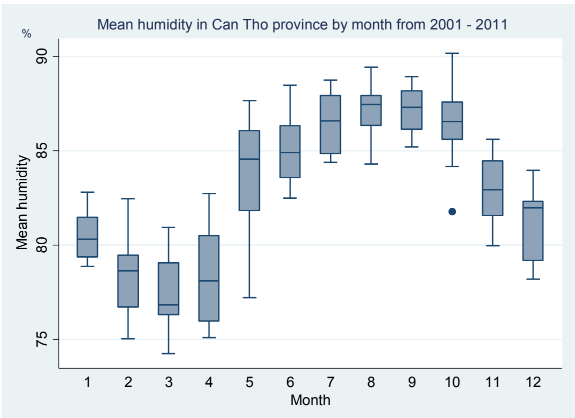
(b)



(c)



(d)



(e)

Figure 2. Climate variables in Can Tho by month (2001 - 2011); (a) mean temperature (°C); (b) maximum temperature (°C); (c) minimum temperature (°C); (d) mean rainfall (mm) and; (e) mean relative humidity (%). In every figure, 12 bars symbolize the data in 12 months. In each bar, the horizontal lines represent (from the top) the maximum, the third quartile, the median, the first quartile and the minimum of data. The shaded box represents the middle 50% of the distribution (between the first and third quartiles). Dots symbolize to outlier values.

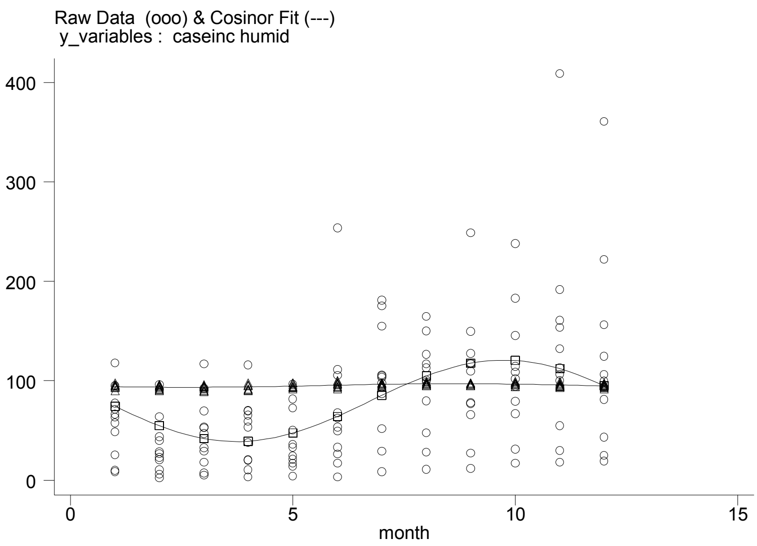


Figure 3. Correlation between dengue hospitalization incidence and relative humidity (2001-2011)

3.2.3. Humidity

Humidity was generally high, averaging 83.6±0.5% (95% CI 82.6 - 84.6%) (Fig. 2(e)). Projecting into the future, it is difficult to assess the trajectory of relative humidity. In earlier climate change models, relative humidity was assumed to remain constant (Dessler and Sherwood, 2009). However, Minschwaner and Dressler (2004) modelled changes in relative humidity in the upper troposphere, and discovered that relative humidity is likely to decrease slightly as temperatures rise. In addition, a study of trends in relative humidity in the USA between 1961 - 1995 showed that surface relative humidity changes varied regionally but increased slightly overall (Gaffen and Ross, 1999). Accurately modelling surface relative humidity in conjunction with other climate variables may be critical for dengue predictions in the face of climate change.

3.3. Dengue hospitalization rates and climate

By examining dengue hospitalization rates and climate variables in a time series analysis spanning 8 years, we have shown here that dengue hospitalization rates in Can Tho are positively correlated with humidity, but not with temperature or rainfall (Fig. 3). Humidity is a key determinant of mosquito longevity (Canyon *et al*., 1999). Humidity also has been associated with movement patterns of *Ae. aegypti* into and out of houses (Suwannachote *et al*., 2009). Furthermore, *Ae. aegypti* fecundity has been shown to be substantially reduced by low humidity (Canyon *et al*., 1999). Experimental studies of the ability of dengue virus to proliferate within *Ae. aegypti* under varying temperatures and relative humidity demonstrated significantly higher dengue virus titers with high humidity. This study also reinforced that mosquito survival was drastically lower in 65% vs 90% relative humidity (20-day survival: 0-45% vs. 90-93%, respectively). With higher relative humidity (90%), larvae developed more quickly, and a greater proportion of pupae emerged as adults compared to lower humidity conditions (Thu *et al*., 1998). Similar positive associations between relative humidity and dengue have been reported elsewhere such as, in New Caledonia, where Descloux *et al.* (2012) reported that a relative humidity above 95% and temperatures exceeding 32°C were important predictors of dengue outbreaks. Johansson *et al.* (2009) demonstrated in Puerto Rico that the effects of climate on dengue transmission are geographically variable.

A study examining regional differences in Vietnam also showed that there is substantial heterogeneity of the influence of weather variables on dengue incidence. In Ho Chi Minh City (180km north of Can Tho), where dengue incidence was highest, a significant positive relationship was observed between relative humidity and dengue incidence, but not for rainfall. A significant negative association was seen for temperature and dengue incidence in this city. This was in contrast to the cooler Ha Noi capital, (1,877km north of Vietnam), where rainfall and temperature were both positively associated with dengue incidence, whereas relative humidity was negatively associated with the outcome (Vu *et al*., 2014).

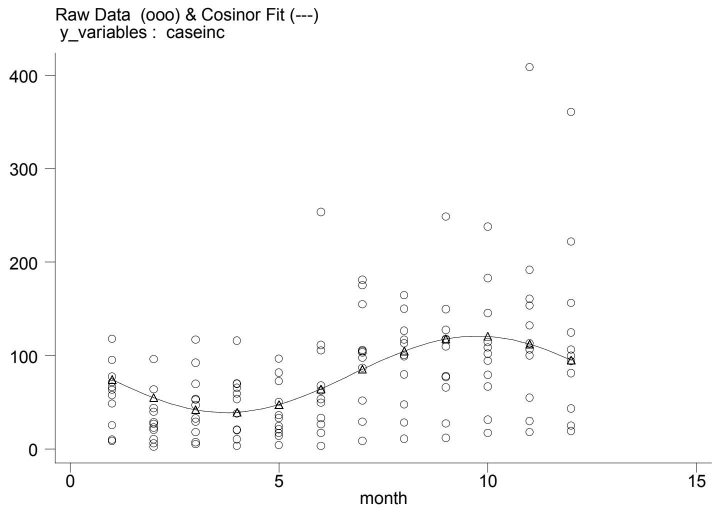


Figure 4. The Cosinor Fit depicts fitted monthly dengue incidence based on observations between 2001 and 2011

Taken together, these factors may explain why only humidity was significantly associated with dengue hospitalizations. It is possible that the temperature and precipitation consistently remained within optimum range for mosquito and viral development over time, and therefore did not reveal a significant association.

3.4 Predicting

Dengue hospitalization rates by month from 2001 to 2011 were shown in a Cosinor fit graph by month (Fig. 4).The graph suggested a seasonal pattern. The Augmented Dickey-Fuller test for unit root indicated that the series was not stationary (12-month lag, MacKinnon approximate *p-value* for *Z(t)=0.1928*). The series became stationary upon differencing for seasonality (Augmented Dickey-Fuller test for unit root, 12-month lag, *p-value=0.0636*). Further term selection for the ARIMA model was accomplished by examining the autocorrelation function (ACF, Fig. 5) and partial autocorrelation function (PACF, Fig. 6) structures of dengue hospitalizations. The PACF cut-off at lag 1 suggests an AR (P=1). The ACF decay at lags 1-2 or 1-3 suggests an MA (Q=2).

Climate variables (maximum temperature, rainfall, and humidity) were then incorporated into the model. Neither rainfall nor maximum temperature were significant, and were therefore dropped. In Table 1 relative humidity was significant with a lag of 1 month (*p=0.042*). Adequacy of the ARIMA model was assessed by examining the ACF of the residuals for white noise (Portmanteau Q-statistic=*37.23*, *p=0.50*; Bartlett's B statistic=*0.72*, *p=0.67*; Fig. 7). These suggest that the residuals are uncorrelated (white), and that the model is therefore adequate.

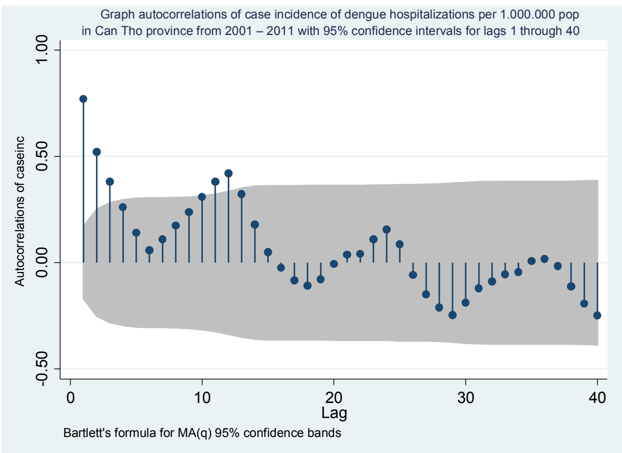


Figure 5. Autocorrelations of dengue hospitalization incidence per 1,000,000 population in Can Tho, 2001 - 2011, with 95% confidence intervals (shaded), and lags 1 through 40

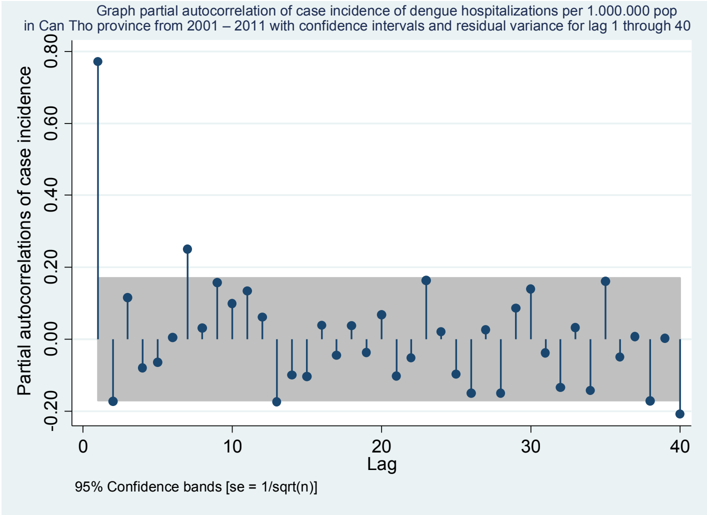


Figure 6. Partial autocorrelations of dengue hospitalization incidence/1 million population in Can Tho 2001 - 2011, with 95% confidence intervals (shaded), and residual variance for lag 1 through 40

For forecasting of dengue incidence and hospitalizations in Can Tho and similar regions, future analysis could incorporate such non-weather factors to account for the influence of human activities on the outcome. As climate modelling improves with the use of increasingly sophisticated tools (e.g. the Atmospheric Infrared Sounder satellite), an analysis that more accurately models changes in relative humidity in relation to rising temperature would be of value to estimate the impact of climate change on dengue incidence in this region.

4. Conclusions

This study shows that dengue hospitalization rates from 2001 - 2011 in Can Tho were positively correlated with humidity, but not with temperature or rainfall. We also have shown here that the ARIMA model-supported maximum relative humidity was significant with a lag of 1 month ($p=0.042$) as an important predictor for dengue hospitalizations in Can Tho, and is consistent with other studies in climatically similar areas. With further validation, this finding may improve dengue prevention and management by helping focus efforts during times of high humidity.

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Table 1. SARIMA model of dengue hospitalizations

Independent variable	SARIMA model	Parameter	Coefficient	Standard deviation	p
Humidity	AR(1), SMA(1, 12)		2.290	1.12	0.042
		AR(1)	0.567	0.096	0.005
		SMA(1, 12)	0.421	0.108	0.005

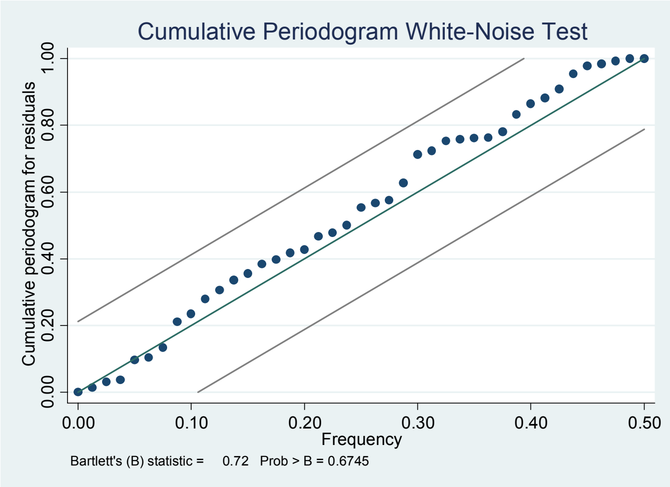

Figure 7. Cumulative periodogram of white noise for residuals

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