Distributed Lag Nonlinear Modelling Approach to Identify Relationship between Climatic Factors and Dengue Incidence in Colombo District, Sri Lanka

Thiyanga Talagala[1]

ABSTRACT

Dengue fever and its deadly complication dengue hemorrhagic fever is an infectious mosquito borne disease. The rise in dengue fever has made a heavy economic burden to the country. Climate variability is considered as the major determinant of dengue transmission. Sri Lanka has a favorable climatic condition for development and transmission of dengue. Hence the aim of this study is to estimate the effect of diverse climatic variables on the transmission of dengue while taking the lag effect and nonlinear effect into account. Weekly data on dengue cases were obtained from January, 2009 to September, 2014. Temperature, precipitation, visibility, humidity, and wind speed were also recorded as weekly averages. Quasi Poisson regression combined with distributed lag nonlinear model was used to identify the association between dengue incidence and climate variables. Results of DLNM revealed; mean Temperature 25°C – 27°C at lag 1 – 8 weeks, precipitation higher than 70mm at lag 1- 5 weeks and 20- 50mm at lag 10 – 20 weeks, humidity ranged from 65% to 80% at lag 10 – 18 weeks, visibility greater than 14 km have a positive impact on the occurrence of dengue incidence while, mean temperature higher than 28°C at lag 6 – 25 weeks, maximum temperature at lag 4 – 6 weeks, precipitation higher than 65mm at lag 15 – 20 weeks, humidity less than 70% at lag 4 – 9 weeks, visibility less than 14km, high wind speed have a negative impact on the occurrence of dengue incidence. These findings help to strengthen dengue prevention and control campaigns.

Key words: Dengue, Distributed Lag Non Linear Modelling, Quasi - Poisson, Climate, Time Series.

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INTRODUCTION

"Small bite – big threat"; the theme of World Health Day, 2014 is a timely reminder of huge harm placed by small vectors, such as ticks, fleas, mites, sand flies and mosquitoes. These animals help to spread a range of vector borne diseases that affect people of all ages across all socio-economic backgrounds. Out of these diseases, dengue is the world's most dangerous viral vector-borne disease transmitted via infective female mosquitoes, namely *Aedes aegypti* and *Aedes albopictus* [1]. The geographic distribution of dengue, both the classical dengue fever (DF) including its deadly complication has been expanded dramatically in recent decades [2]. According to current estimates, this disease is now endemic in more than 100 tropical and subtropical countries [3].

Many factors influence the dynamics of dengue transmission and infection such as climate variability, physical environment and social factors [4]. But climate variability is considered as an major determinant of dengue epidemics [5]. Temperature, humidity, and rainfall have been reported to affect the occurrence of dengue incidence either through changes in vector survival, life span of mosquitoes, or human interaction [6]. *Aedes* mosquitoes take approximately 1-2 weeks or longer to complete their life cycle depending on temperature, and availability of water, and other climatic factors. The average life length of a mosquito ranges from 2 to 4 weeks [7]. A study conducted by Hii et al. (2013) found given the optimal environmental condition *Aedes* mosquitoes can live approximately 100 days. Further *Aedes* can lay eggs on a dry surface and these eggs can survive complete dryness for several months depending on humidity [6, 7]. Rainy seasons create ample number of artificial and natural habitats for *Aedes* mosquitoes and it also increases the mortality rate of adult mosquitoes [6 - 8]. But heavy rainfall flushes away dengue breeding sites.

To date, there is still no effective vaccine available to control the occurrence and periodic recurrent outbreaks of Dengue. In the absence of a vaccine for the prevention and control of dengue fever, eliminating the breeding places of *Aedes* mosquitoes is still the only effective strategy to interrupt the transmission of the disease. To strengthen vector control campaigns health officials need to know much more about the patterns of dengue virus transmission and the climatic conditions that underlie these patterns.

Generalized Linear Models (GLM) or Generalized Additive Models (GAM) with Poisson distribution has been used to estimate association between meteorological factors and mortality or disease incidence [5]. But GAM/GLM are not appropriate to fit for time series data because they require the data to be independent. Moreover, lag effect of climate variables may influence the occurrence of dengue outbreaks [9]. Therefore, our study has been designed to estimate the effect of diverse climatic variables on the transmission of dengue fever while taking the lag effect and nonlinear effect into account.

MATERIALS AND METHODS

Data Description

Epidemiological data

Weekly notified dengue cases in 25 districts in Sri Lanka were obtained from weekly epidemiological reports published by the Epidemiology Unit, Ministry of Health, Sri Lanka. Data include cases from 1st week of (January) 2009 through 36th week (September) of 2014.

Climatic data

Daily meteorological data were obtained from an online source (www.tutiempo.net/en/). The data from this source was obtained directly from the local weather station in Colombo. Daily mean, minimum and maximum temperatures, mean visibility, mean wind speed, maximum sustained wind speed, relative humidity and precipitation for the period 2009, January 2013, September were obtained. The daily values were used to obtain weekly averages.

Study Area

The association between dengue incidence and climatic factors were studied in Colombo district, where there is a marked increse of dengue cases evidenced during the last few years. It is located in the southwest of Sri Lanka and has an area of 699km^2. Colombo district is the most urbanized and density populated region of Sri Lanka. The main features of the climate are the relatively stable temperature aand high humidity year-round, forming an ideal condition for the growth of the vector of dengue fever mosquitoes.

TABLE 1

CLIMATE VARIABLES, VARIABLE LABEL AND UNIT OF MEASUREMENT

CLIMATE VARIABLE	VARIABLE LABEL	UNIT OF MEASUREMENTS
Mean Temperature	TEM	°C
Maximum temperature	TM	°C
Minimum temperature	Tm	°C
Mean humidity	H	%
Precipitation amount	PP	mm
Mean visibility	VV	km
Mean wind speed	V	km/h
Maximum sustained wind speed	VM	km/h

TABLE 2

CHOICE OF LAG PERIOD, VARIABLE BASIS AND LAG BASIS

VARIABLE	LAG PERIOD (WEEKS)	BASIS FOR VARIABLE	BASIS FOR LAG
Mean Temperature	30	ns with degree 1	ns with lagnots
Maximum Temperature	30	ns with degree 1	ns with lagnots
Precipitation	25	B-spline with degree 4 and 5 df	Polynomial with degree 3
Humidity	20	ns with degree 2	ns with lagnots
Maximum sustained wind speed	20	ns with degree 2	ns with lagnots
Visibility	20	ns with degree 2	ns with lagnots

Statistical Analysis

Overdispersion was observed in dengue data. Hence Quasi-Poisson regression model combined with distributed lag non-linear model (DLNM) was used to examine the effects of climate variables on dengue incidence. The objective of developing the DLNM model are to justify the impact of lag effect of climate on dengue incidence and to identify the structure of the lag-period for different climate variables and to capture the nonlinear nature of the data by introducing appropriate smoothing techniques.

DLNM, was introduced by Gasparrini et al. (2010) [10] is a flexible model to describe simultaneously a non-linear and delayed effect of climate change on dengue incidence. This model used a "cross-basis" function that examine a two dimensional relationship along the dimensions of climate change and lag weeks. The cross-basis is specified by the choice of two basis, one for each dimension, among a set of possible options such as splines, polynomials, or step functions. In our study, the choice of lag period is varies for various meteorological factors. We decided the lag period based on the literature review and provided the maximum plausible weeks as the lag for all the variables to improve the precision of the DLNM model. Table 2 summarizes the choice of lag period, variable basis and basis for lag for each climatic variable. Except for precipitation, in this study, we used natural spline (ns) basis for all the variables used in the model. B-spline function was used as the basis function for precipitation while polynomial function was used as the basis for lag. The degree of freedom for all variable basis and lag basis are based on the results of exploratory data analysis, previous studies from literature and also judging by the AIC/ BIC results tested under various values of degree of freedom. In this analysis we placed the knots of variables at equally spaced values on the log scale of lags.

The applied Poisson model can be written as follows.

$$Ln(E(Y_t)) = \alpha + \beta_1 TEM_{t,l} + \beta_2 TMAX_{t,l} + \beta_3 PP_{t,l} + \beta_4 H_{t,l} + \beta_5 VM_{t,l} + \beta_6 VV_{t,l} + \mu_j week_j + \gamma_k year_k$$

Where t refers to the week of the observation; (Y_t) denotes the observed weekly dengue counts on week t; α is the model intercept. $TEM_{t,l}$, $TMAX_{t,l}$, $PP_{t,l}$, $H_{t,l}$, $VM_{t,l}$, and $VV_{t,l}$ the cross basis matrix obtained to mean temperature, maximum temperature, precipitation, humidity, maximum sustained wind speed and visibility respectively. β_i's represent the vector of coefficients for corresponding cross basis and l is the lag weeks. $Week_j$ (j= 1, 2, 3, ...52) denotes week effects that were controlled by a categorical variable $year_k$ denotes the year (k=2009, 2010, 2011, 2012, 2013, 2014).

Since the annual population growth rate in Colombo district is below 1%, the population was relatively stationary during the time period 2009 – 2014 (According to 2001 census Colombo district population 2251300, 2012 census population in Colombo district equals 2310100, population growth from 2001 to 2012 is 2.61%). Hence we used the dengue counts as the response variable in our model. Finally the residuals were checked to evaluate the adequacy of the model. Sensitivity analyses were performed by varying the degrees of freedom (df). All statistical analyses related to DLNM were performed with R software version 3.1.3 using the package dlnm.

RESULTS

In the total 298 weeks of the study period, there were 36949 dengue cases (including Dengue and Dengue Hemorrhagic fever) reported in Colombo District. Figure 1 shows the time series plot of dengue cases in Colombo District. Figure 1 tends to exhibit repetitive behaviour, with regular seasonal pattern. Dengue disease dynamic pattern indicates that the critical months of dengue were during May – September, which is the south west monsoon season. Descriptive statistics of climate variables for the study period are shown in Table 3. Variation in precipitation is higher than the other climatic variables.

Pearson's correlation analyses between all meteorological variables were assessed. According to table 4 there is a strong linear relationship between minimum temperature and mean temperature. Further, there is a strong linear relationship between mean wind speed and maximum sustained wind speed. Hence minimum temperature and mean wind speed were not included in the DLNM framework in order to avoid multicolinearity.

The model selection is still a problem within the DLNM framework [11]. Studies based on simulations have shown good performance of methods based on the Akaike information criterion. Hence the model with minimum QAIC (= 8159.779) and QBIC (=15483.04) was selected. Residual analysis was used to evaluate the adequacy of the model to ensure the assumption of normality and independent of error terms (Figure 2).

Three-dimensional plots of figure 3 show the relationship between meteorological variables and the relative risk (RR) of dengue with various lag weeks. For better interpretative purpose, we plotted specific contour plots of the associations. All the relationship curves were nonlinear, whereas the different variables had different characteristics. Relative risk is defined as "the ratio of the probability of dengue incidence occurring at a certain value of a weather variable to the probability of the event occurring at a reference value of the same weather variable" [12]. The change of reference may affect the width of confidence interval but it will not affect the RR curve itself. Hence median of each climate variable was chosen as the reference value.

Overall, the estimated effect of climatic variables on dengue was nonlinear. A visual inspection of the figure 3 suggests that there was an immediate harmful effect of low mean temperature (<27^{0}C) on dengue incidence at lag 4-9 weeks, and a protective effect (RR<1) of low temperature at lag 10-25 weeks. The three-dimensional plot of maximum temperature show the impact of maximum temperature on dengue incidence is completely reverse of the behavior of mean temperature.

In general, it can be seen that a higher precipitation was associated with a higher dengue incidence, but this observed relationship does not hold true when precipitation is 25mm -65mm at lag 5- 25 weeks. The strongest effect of rainfall occurred at lag 0-5 weeks with more than 60mm precipitation, and lag 15-20 weeks with 40-50 mm precipitation. Very high precipi-

FIGURE 1

TIME SERIES PLOT OF DENGUE CASES IN COLOMBO DISTRICT, 2009 JANUARY – 2014 SEPTEMBER

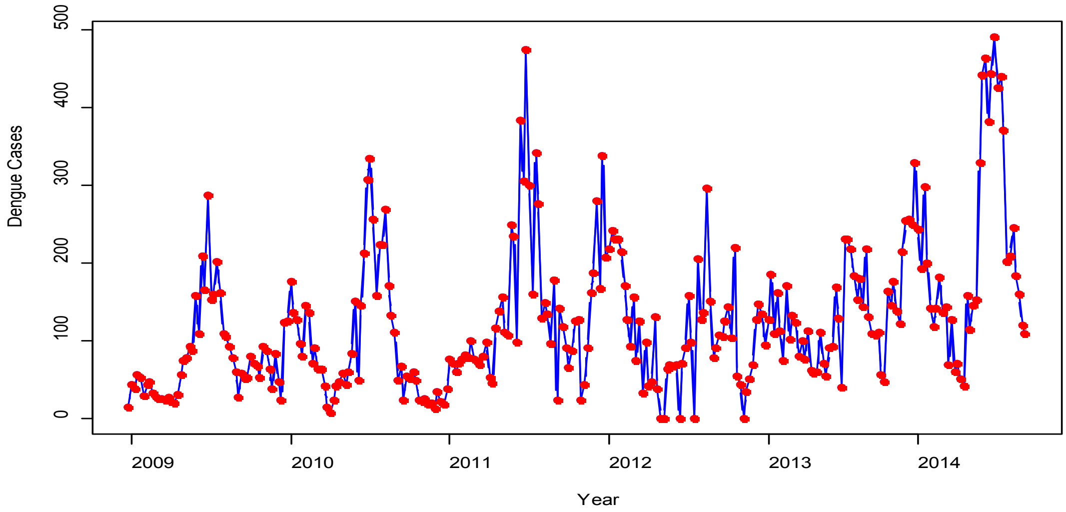


TABLE 3

DESCRIPTIVE STATISTICS OF CLIMATE VARIABLES: JANUARY, 2009 – SEPTEMBER, 2014

	MINIMUM	MEDIAN	MEAN	STANDARD DEVIATION	MAXIMUM
T	24.186	27.723	27.705	0.899	29.657
Tmin	20.829	24.979	25.021	1.336	28.043
Tmax	27.314	30.871	30.911	0.905	33.714
H	62.000	80.000	79.624	4.410	90.286
PP	0.000	2.994	6.193	9.539	71.340
VV	10.943	19.736	19.478	0.897	20.286
V	0.850	5.157	5.215	1.806	14.386
VM	4.600	10.143	10.559	3.066	29.686

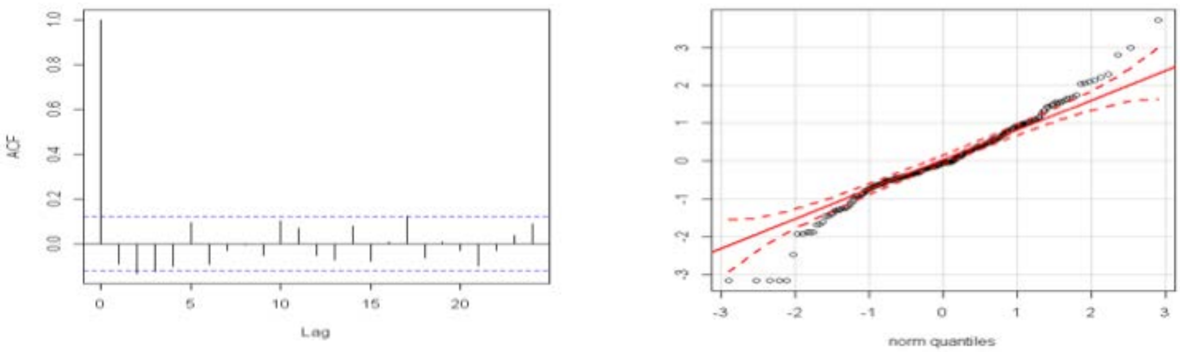
TABLE 4

PEARSON'S CORRELATION COEFFICIENTS MATRIX OF METEOROLOGICAL VARIABLES IN COLOMBO DISTRICT, SRI LANKA, JANUARY, 2009 – SEPTEMBER, 2014

	T	TMAX	TMIN	H	PP	VV	V
TMAX	0.531						
TMIN	**0.814**	0.040					
H	-0.127	-0.584	0.221				
PP	-0.198	-0.199	-0.141	0.483			
VV	0.335	0.169	0.250	-0.214	-0.307		
V	0.220	-0.068	0.355	-0.240	-0.253	-0.059	
VM	0.096	-0.024	0.122	-0.139	-0.091	-0.113	**0.750**

FIGURE 2

ACF PLOT OF RESIDUALS AND NORMAL PROBABILITY PLOT OF RESIDUALS;
KOLMOGOROV-SMIRNOV TEST (P = 0.206)



tation (>70mm) at lag 15-20 weeks reduce the relative risk of dengue incidence. Further the precipitation around 30-60mm at lag 0-3 weeks has a protective impact on the occurrence of dengue incidence. Humidity around 60-75 mm has a positive effect on dengue incidence around lag 10-18 weeks. High humidity (>85%) has a protective impact on dengue incidence. The estimated effect of wind visibility on dengue cases differed for low and high visibility. The risk of dengue transmission increases with visibility. Low visibility (<14 km) has a negative impact on the occurrence of dengue incidence while the high visibility (> 15km) a positive impact on increase of dengue incidence. Maximum sustained wind speed (> 25km) at lag 0-10 weeks has a slight positive impact on increase of dengue incidence.

DISCUSSION

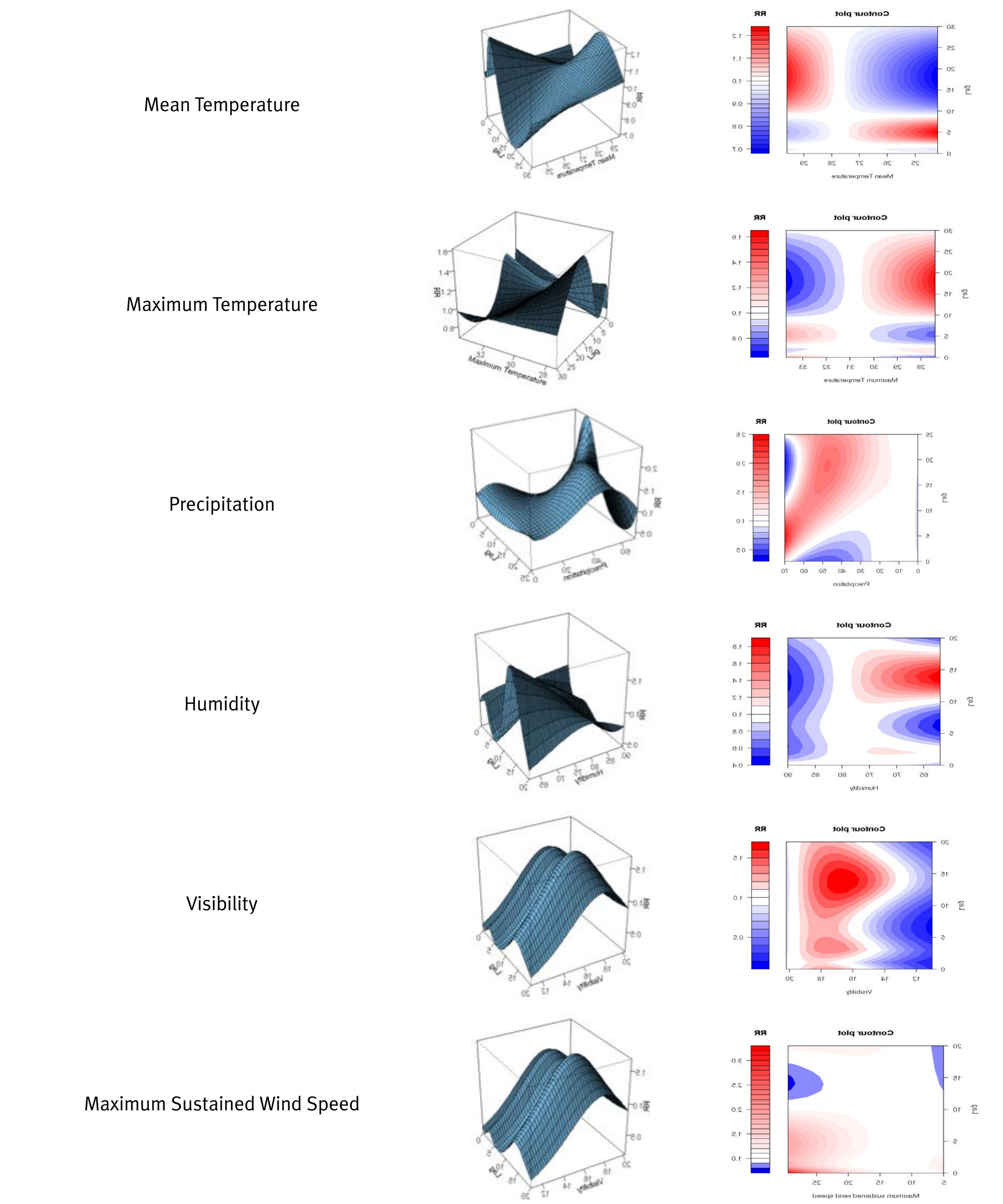
Results of distributed lag nonlinear model revealed mean temperature around 25^{0}C – 26^{0}C prior to 5 weeks and 28^{0}C – 29^{0}C temperature prior to lag 10 – 25 weeks , high precipitation (>30mm), humidity 65% - 75% prior to lag of 10-15 weeks and high visibility(> 16km) have an harmful impact on increasing relative risk of dengue incidence. Rainfall season is positively associated with high dengue incidence. This is line with the studies that reported the highest risk of dengue cases related to rainfall in Mexico, Brazil [13]. Rainfall influences the abundance of dengue vectors and aquatic populations (eggs, larvae, and pupa). Increased rainfall supports more suitable breeding sites for the immature development of the aquatic population. Further very high rainfall (> 70mm) at lag 15 – 20 weeks and rainfall between 30mm – 60mm have a protective impact on the occurrence of dengue incidence. Rainfall directly influences the density of the mosquitoes, however, strong rainfall causing floods may results in the disappearance of small ponds and thereby the feasible places for mosquito breeding [10]. Hence, the impact of rainfall on mosquito growth and distribution should be viewed within the geographical location of the study area. For example, if the region under consideration is a plain area with appropriate and fully covered sanitation systems, mosquito breeding may be less, while, if the region is an area where water remains stagnant for days, the area would be more vulnerable to a rapid increase in mosquito population due to rain. According to the results of distributed lag non linear model we observed high visibility being associated with high dengue notifications. Although it is not established whether this association is causal, high visibility could help the mosquito movements and biting behaviors.

CONCLUSION

In conclusion, Mean Temperature 25^{0}C – 27^{0}C at lag 1 – 8 weeks, Precipitation higher than 70mm at lag 1- 5 weeks and 20- 50mm at lag 10 – 20 weeks, humidity ranged from 65% to 80% at lag 10 – 18 weeks, visibility greater than14 km have a positive impact on the occurrence of dengue incidence while, Mean Temperature greater than 28^{0}C at lag 6 –

FIGURE 3

3D PLOTS AND CONTOUR PLOTS OF EFFECT OF CLIMATIC VARIABLES ON RR OF DENGUE INCIDENCE



25 weeks, maximum temperature at lag 4 – 6 weeks, Precipitation higher than 65mm at lag 15 – 20 weeks, Humidity less than 70% at lag 4 – 9 weeks, Visibility less than14km, high wind speed have a negative impact on the occurrence of dengue incidence.

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