THE INFLUENCE OF CLIMATIC FACTORS ON DENGUE EPIDEMIES IN THE CITIES CUIABÁ (MATO GROSSO STATE) AND LAVRAS (MINAS GERAIS STATE), BRAZIL, USING STATISTICAL METHODS

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- *ABSTRACT: Dengue is one of the main problems of public health in the world. It is estimated that about 2.5 billion people are now at risk of dengue. Given this current context of the disease, we have developed a model of temporal series in an attempt to identify the climatic factors that contribute to the spread of dengue in the cities Lavras (Minas Gerais state) and Cuiabá (Mato Grosso) in Brazil. The series for analysis were the number of dengue reported cases, series of minimum, mean and maximum temperature, relative humidity of air, and rainfall index. Models better adjusted to the data according to the methodology of Box and Jenkins and a regression model that relates dengue cases and climatic factors were found. In Cuiabá, rainfall and maximum temperature influence the number of dengue cases, while in Lavras, besides rainfall and maximum temperature, mean temperature and humidity influence. The determination coefficients R2 in Cuiabá and Lavras were 0.31 and 0.68, respectively. In the second set for Lavras, we consider the series of maximum and minimum temperature and precipitation with an R2 of 0.67, and the maximum temperature and precipitation kept influencing the number of dengue cases. It was not possible to propose a single model to explain the behavior of the number of dengue cases for the two cities. This may be strongly related to climate variability. However, both models have a common component, which is the influence of maximum temperature with a lag of four months.*

- *KEYWORDS: Time series; dengue; climate.*

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1 Introduction

The climate is one of the environmental elements that influence men. From the XIX century, concerns on studying the climate have intensified due to the phenomenon of urbanization and the consequent populational sprawl (BRANDÃO AND RUSSO, 2002).

Among all the environmental problems, changes in climate are arousing greater concern. The incidence of determined diseases is directly related to the tropical areas of some regions and climatic zones, because they provide favorable conditions for the proliferation of insects that transmit diseases.

Dengue is one of the main problems of public health. According to the World Health Organization it is estimated that 2.5 millions of people are now at risk of dengue.

The first epidemy of dengue with confirmation in laboratory in Brazil occurred in 1982, in Boa Vista (Roraima state). From 1986, several Brazilian states reported the occurrence of epidemic peaks. Rio de Janeiro state recorded 95,000 cases and approximately 3 million people infected (FIGUEIREDO, ET. AL., 1990). In the last 20 years, several dengue epidemies in all regions of Brazil were recorded due to spread of the virus vector and transmitter.

The Secretary of Health Surveillance, in collaboration with the State and Municipal Secretary of Health reported in 2014 for Brazil 215.169 dengue cases from January to April 5, 2014 the Southeast region has the highest number of reported cases (109 843 cases, 51%), followed by the Midwest (50 800 cases, 23.6%), Northeast (19,689 cases, 9.2%), South (19 268 cases, 9.0%) and North (15,569 case, 7.2%)

Dengue is considered the most widespread human arbovirus in the world. The Arboviruses multiply in the tissues of arthropods, which are infected, becoming vectors after sucking the blood of hosts in the period of viremia (HALSTEAD, 2007). It is an acute febrile illness caused by dengue virus (DENV), an arbovirus belonging the family Flaviviridae, genus Flavivirus, with four distinct serotypes, DENV-1, DENV-2, DENV-3 and DENV-4.

These viruses are transmitted to humans by mosquitoes of the genus Aedes, and the main vector is Aedes aegypti. Transmission of the virus in its simplest form, involves the ingestion of blood containing the virus by the mosquito, and its passage to a second susceptible human host (GUBLER, 1995).

It is generally observed a seasonal pattern of dengue incidence in Brazil, coinciding with summer due to the highest rainfall and increased temperatures, factors that favor the increase of infestation indexes and vector density. Nevertheless, outbreaks of dengue fever may also occur during the dry period, and may be related or not, with the increase in vector population (GUBLER, 1997)e (HALSTEAD, 1997).

Thus, the humidity and temperature of the environment have an effect on transmission of the virus. During the rainy season, due to high humidity, mosquito survival is longer although in some regions mosquitoes are most abundant in the dry season, when rain occurs fast and sparse. The formation of small puddles helps the hatch of the dried eggs and the rapid increase adult form of mosquitoes (RODHAIN AND ROSEN, 1997).

This study aims to develop a temporal model of series and regression in an attempt to identify the climatic factors that contribute to the spread of dengue in the city of Lavras (Minas Gerais state) and Cuiabá (Mato Grosso state). Seasonal ARIMA models were used for the series, specifically the approach used Box-Jenkins (MORETTIN E TOLOI, 2006) and the construction of a multiple linear regression model (CHARNET ET. AL. 1999).

2 Methodology

The series to be considered for analysis are historical series of the cities Lavras in Minas Gerais state and Cuiabá in Mato Grosso state. The choice of these cities was done because of the easy achievement of data and because they represent different climates and regions in Brazil. Figure 1 shows the map of the two cities under study in Brazil.

Figure 1 - Location of Lavras (Minas Gerais) and Cuiabá (Mato Grosso).

Lavras is located in the South of Minas Gerais state, it has an area of 564.5 km^2. Its geographical position is determined by 21^o $14'$ $30''$ S and 45^o $00'$ $10''$ W. It is 919 meters above sea level. The climate of Lavras is classified as mesothermal (KÖPPEN, 1948), with mild and rainy summers. The mean annual temperatures is about $19,3^oC$ ranginf from 113, 5^oC to $27,8^oC$. The mean rainfall is 1,411 mm. In the estimates for 2010 by the Brazilian Institute of Geography and Statistics (IBGE), Lavras has 92,171 inhabitants.

Cuiabá is located in the Midwest, it is the capital of Mato Grosso state. It represents the geodesic center of South America, located in the geographic coordinates 15^o $35'$ $56''$ S and 56^o $06'$ $01''$ W, at an altitude of 151 meters above sea level. According to estimates made for IBGE 2010, the population of Cuiabá is 551,350 inhabitants. The mean temperature is about 24^oC. The climate is tropical and humid. The mean annual rainfall is 1469.4 mm. The mean maximum temperatures reach 35^oC, but the absolute maximum can reach 40^oC in the warmer and muffled months. The minimum temperaturein July, the coldest month, is 16^oC to with thermal sensation of 11^oC. The climate is classified as tropical semi-humid.

2.1 Data collection

This study considered the number of reported cases of dengue fever, temporal series such as minimum ad mean temperature, relative air humidity, and rainfall index in the city of Lavras, Minas Gerais. The series of dengue cases in the city of Lavras were provided by the Department of Health, Sector of Epidemiology of Lavras. Climatic data were provided by the climatology Sector of the Engineering Department, Universidade Federal de Lavras (UFLA). Data were considered monthly from January 2001 to December 2009.

For Cuiabá we considered the series of number of dengue reported cases in this city and climatic series such as minimum and maximum temperature and rainfall. The number of dengue cases in Cuiabá was provided by the Department of Health, Epidemiology sector, the Municipality of Cuiabá. The climatic data were provided by the National Institute of Meteorology (INMET). The data were collected monthly from January 2001 to December 2009.

2.2 Processing and data analysis

We analyzed each series from 2001 to 2009 using Box-Jenkins approach to the ARIMA seasonal modeling of the series which consists of the following process:

1. Analysis of the graph of the original series and the graph of amplitude as a function of the mean, making sure if its is necessary the transformation of data;

2. Analysis of the series and its function of autocorrelation, checking the evidence for trends and seasonality;

3. Verifying the existence of trends and seasonal components through the application of the signal test and Fisher's exact test, respectively;

4. Realization of the number of differences necessary to remove the deterministic trend and seasonality of series;

5. Analysis of the function of autocorrelation (ACF) and partial autocorrelation (PACF) of the differentiated series (free trend and / or deterministic seasonality);
6. Fit of the model and verification of significant estimates;
7. Testing the waste from the residue ACF of the fitted model to see if the residue is white;
8. For the case of more than one model adjusted for the series, we applied the criteria of Akaike and EQMP to choose the best model that fits the data;
9. Identification of the mathematical model with estimated parameters.

Then, for the regression model of the cities of Cuiabá and Lavras we used the residues from the adjusted model for each series in a study in which the dependent variable was the residue of dengue cases and variables waste were independent of the models adjusted for maximum, mean and minimum temperature, humidity and precipitation.

Through the Backward method lags of 1 to 6 months was added in each climatic series, and analyzing the p-value we withdrew the variables that had the highest p-value to obtain a regression model of series residues.

For statistical analysis of data the program Gretl 1.9.2 was used. Gretl (Gnu Regression acronym, Econometrics and Time-series Library) is a free software that collects and interprets econometric data, this software enables you to do a full analysis of temporal series, from graphical analysis of the data to forecasts.

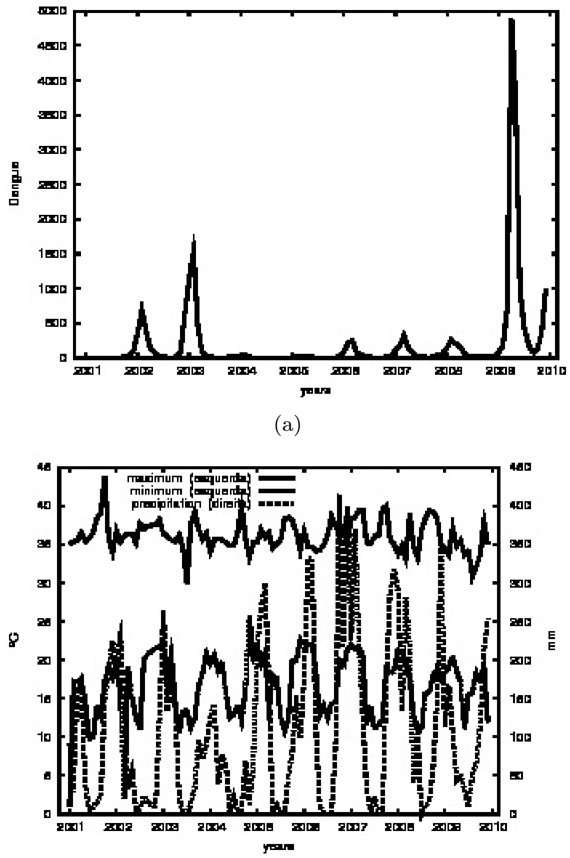
3 Results

The analysis of the series under study was initiated from a visual inspection of our graphics. It can be seen in Figure 2 e 3 that shows the graphs of all series under study in Lavras and Cuiabá.

In order to verify the need of a transformation in the series, we used the plot of amplitude versus average. The series were divided into groups of 12 consecutive observations, as seen in Morettin and Toloi (2006), because the data were considered monthly. The average was directly proportional to the amplitude in the two sets of dengue cases in the cities of Cuiabá and Lavras, indicating the need for a logarithmic transformation to stabilize the variance of the data.

The logarithm graphs of monthly series of dengue cases in the cities of Lavras and Cuaibá can be seen in Figure 4.

The climatic series did not need transformation of data. Through preliminary analysis that were performed, it was confirmed that the series did not present trends and seasonality. This way, it was necessary to differentiate the series in order to make them stationary. It was applied a difference in the series, $lag = 12$ to remove seasonality. After these adjustments and based on the methodology of Box and



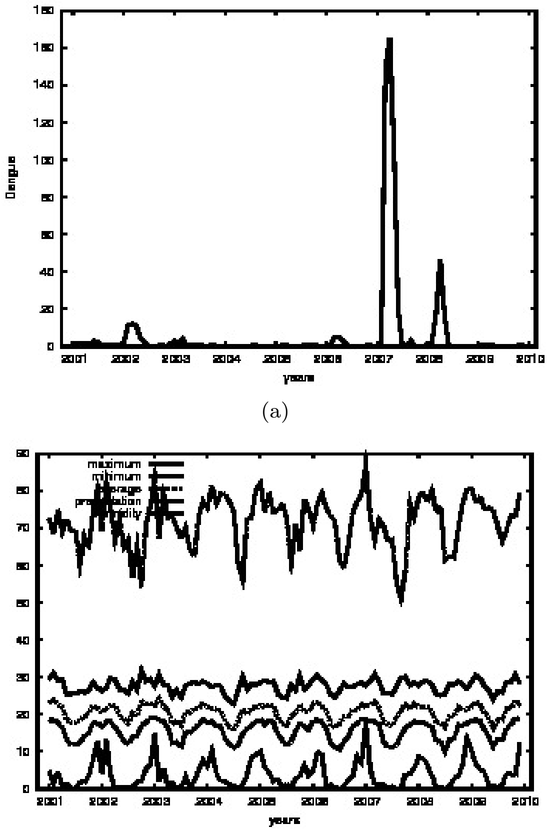
(a)

(b)

Figure 2 - Dengue Cases Cuiabá 2001 to 2009 (a) Climate series 2001 to 2009 Cuiabá (b).

Jenkins, the identification of the model that fits the data was performed through the ACF and PACF of the stationary series in each series.

According to the functions of autocorrelation and partial autocorrelation models that have been proposed for the series, the Table 1 presents the series of models for the city of Cuiabá, and models for the series of Lavras can be seen in Table 2.



(a)

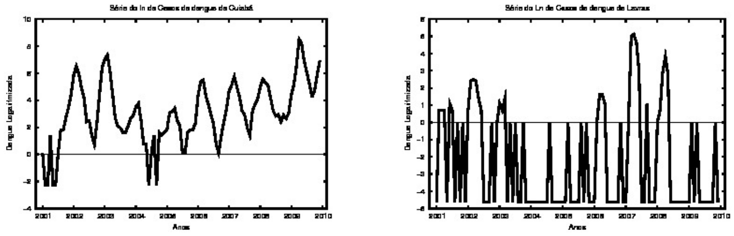
(b)

Figure 3 - Dengue Cases Lavras 2001 to 2009 (a) Climate series 2001 to 2009 Lavras (b).

Table 1 - Series models for climate found the city of Cuiabá-MT

Time series	Models SARIMA
Cases of Dengue	$SARIMA(1,0,0)\text{x}(1,1,0)_{12}$
maximum temperature	$SARIMA(1,0,0)\text{x}(0,1,1)_{12}$
minimum temperature	$SARIMA(0,0,0)\text{x}(0,1,1)_{12}$
precipitation	$SARIMA(1,0,0)\text{x}(0,1,1)_{12}$

After the study of individual series, we found a SARIMA model that better set the data of each one. Thus, the SARIMA model estimated values for all series. Then we created new series, with the actual values minus the estimated value, and we obtained the residues of the adjusted models for each series under study.



(a) (b)

Figure 4 - Ln the monthly series of dengue cases in the city of Cuiabá, from January 2001 to December 2009 (a) monthly series of dengue cases in the city of Lavras, from January 2001 to December 2009 (b).

Table 2 - Series models for climate found the city of Lavras-MG

Time series	Models SARIMA
Cases of Dengue	$SARIMA(7,0,1)\text{x}(1,1,1)_{12}$
maximum temperature	$SARIMA(1,0,1)\text{x}(2,1,0)_{12}$
average Temperature	$SARIMA(2,0,1)\text{x}(2,1,0)_{12}$
minimum temperature	$SARIMA(2,0,1)\text{x}(2,1,0)_{12}$
moisture	$SARIMA(1,0,1)\text{x}(1,1,1)_{12}$
precipitation	$SARIMA(0,0,1)\text{x}(1,1,1)_{12}$

The regression model consisted of the dependent variable as residue of dengue cases and variables waste being independent of the adjusted models of climate variables for each city, through the method Backward. We began considering the procedure for all covariates the lag of 1 to 6 months and then eliminating the non-significant.

According to Table 3, the significant covariables for the regression model for the city of Cuiabá were precipitation and maximum temperature, with a lag of four months for maximum temperature and lags of 3 and 5 months for precipitation. Table 4 shows the significant covariables for the regression model in the city of Lavras, which were maximum temperature, mean humidity and precipitation with a delay of 4 months for maximum temperature and mean lag of six months for humidity and gaps of 2, 3 and 4 months for precipitation. For the model found, only the minimum temperature was not significant.

After adjusting the model, analysis of independence and normality of residuals were conducted for both models. For independence it was made the Durbin-Watson presented value and value for Lavras 1.856275 1.803514 Cuiabá, close to 2, confirming that the residuals are independent.

Considering a second model for the city of Lavras, using only the co-variables model Cuiabá, or residues of maximum and minimum temperature and rainfall, the parameters for this model are presented in Table 5.

Table 3 - Estimates of the parameters of regression model for Cuiaba-MT

parameter	coefficient	Standard Error	p-value
$constant$	98,2603	96,0181	0,3090
$maximumtemperature_{t-4}$	-47,4357	23,1451	0,0435 **
$precipitation_{t-3}$	-1,37109	0,595034	0,0236 **
$precipitation_{t-5}$	1,16675	0,566269	0,0424 **
R^2	0,312083		

significance ** 0,05

Table 4 - Estimates of parameters of the regression model for Lavras-MG

parameter	coefficient	Standard Error	p-value
$constant$	2,58776	4,13920	0,5335
$maximumtemperature_{t-4}$	6,78627	1,72472	0,0002 ***
$averagetemperature_{t-4}$	-7,42233	2,25305	0,0014 ***
$moisture_{t-6}$	0,472335	0,21198	0,0285 **
$precipitation_{t-2}$	3,16057	0,64735	4,79e-06 ***
$precipitation_{t-3}$	2,88671	0,82626	0,0008 ***
$precipitation_{t-4}$	2,53772	0,68206	0,0004 ***
R^2	0,681713		

significance ** 0,05; ***0,01

Table 5 - Estimates of the parameters of the second regression model for Lavras-MG

parameter	coefficient	Standard Error	p-value
$constant$	3,00692	4,09474	0,4647
$maximumtemperature_{t-4}$	2,54011	0,91542	0,0068 ***
$minimumtemperature_{t-5}$	4,61346	1,61943	0,0055 ***
$minimumtemperature_{t-6}$	3,26139	1,62961	0,0485 **
$precipitation_{t-2}$	3,34233	0,68357	4,65e-06 ***
$precipitation_{t-3}$	3,11080	0,86432	0,0005 ***
$precipitation_{t-4}$	2,35556	0,69902	0,0011 ***
R^2	0,67		

significance ** 0,05; ***0,01

Figures 5 and 6 show graphs of the normality test. Both have an outlier, these outliers were studied and Lavras represents the large peak of the dengue epidemy in 2007 and in Cuiabá it represents the peak of the epidemy in 2009. Disregarding these values, the figures show that the residues are normal.

After adjusting the model, analysis of independence and normality of residuals were conducted. For independence the test Durbin-Watson was made and presented value of 1.859220, which is close to 2, confirming that the residuals are independent.

Figure 7 shows the graph of the normality test. Disregarding the value that represents the year 2007, it shows the normality of the residuals.

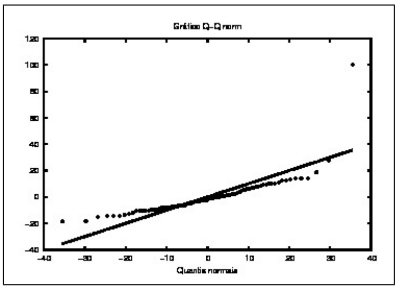


Figure 5 - Chart of the normality of the residuals of the regression model adjusted for the city of Lavras.

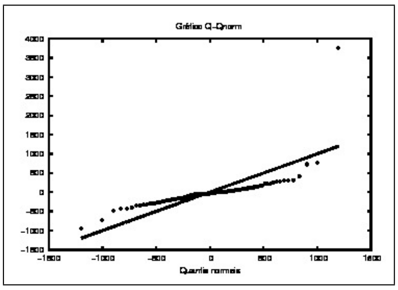


Figure 6 - Graphic of the normality of residues of regression model adjusted for the city of Cuiabá.

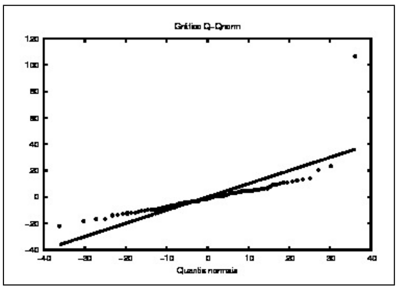


Figure 7 - Graphic of residues normality of the seconde adjusted regression model for Lavras.

The first complete model presented an R^2 of 0.68 and a second model for Lavras R^2 of 0.67. Looking these values of R^2, we noticed that the difference from the first to the second is very small, even using two series over the first model.

4 Discussions

Dengue is strongly related to climatic factors. Several studies show this relationship, that the epidemy of dengue is related to rainfall in Singapore (CHUNG AND PANG, 2002). They considered that the incidence of dengue was negatively correlated with monthly temperature and was inversely related to the relative humidity in Taiwan (WU ET.AL., 2007).

For the study of Cuiabá we found that dengue cases are related to rainfall and maximum temperature. The ideal temperature for the survival of adult mosquitoes is between 15 e 30^0C (YANG ET. AL., 2009). In Cuiabá maximum temperature ranges from 29 to 43^0C, what may explain the negative influence of temperature on the model.

From the analysis of climatic variables, we can observe that the temperature is crucial in dengue epidemies because it affects the rate of development in different life stages of the mosquito, and consequently of the development of dengue virus (THU ET. AL,1998).

Studies in Puerto Rico found that dengue cases are positively correlated with temperature, but only weakly associated with rainfall and with the index of the El Nino Southern Oscillation (ENSO) (JURY, 2008). In Mexico, a study showed that the incidence of dengue increased 2.6 % one week after each increase of 1^0 and the maximum temperature increased by 1.9 % two weeks after each increase of 1 cm weekly rainfall in (GUZMÁN AND KOURÍ, 2002) e (HALES ET. AL., 2002).

For Lavras two models were estimated, the first series using the climate of maximum, mean and minimum temperature, rainfall and humidity. This model showed the positive influence of maximum temperature, humidity, rainfall, and a negative influence of high temperatures. The maximum temperature ranges from 21^0 to 31^0C, the ideal range for survival of the mosquito. In addition, humidity is needed for the breeding of mosquitoes and needs to be studied with more attention.

In the Caribbean the temperature was also statistically significant in the incidence of dengue fever with delay of several months (AMARAKOON ET AL., 2008). Similar lags were observed by Wegbreit in relation to dengue in Trinidad and Tobago (WEGBREIT, 1997), and similar proposals in relation to lags and the epidemy of dengue in Southeast Asia (FOCKS EL. AL., 2003).

For comparison, we made a model using only the series of maximum and minimum temperature and rainfall, as done for the city of Cuiabá and we found a model in which dengue cases had a positive influence in all the lagged series, with maximum temperature with lag 4, minimum temperature with lags 5 and 6, and 2, 3 and 4 for precipitation. Therefore, the models in this work varied among regions, because they depend on the climatic series which presented completely different values for the maximum, minimum temperature and rainfall in each region.

In addition to these climatic variables, we observed that wind power has influence on the flight and dispersion of arthropods, and may be responsible for the introduction of an arbovirus in a non-endemic area, or a sudden reappearance of an arbovirus after a period of absence (REITER, 1988). Despite the movement of air plays an important role in the transport of infected vectors, the wind can also reduce the ability to fly and the mosquito contact with humans (HOFFMANN AND MILLER, 2002). Kennedy in one of the studies that showed that the wind speed of more than 150 cm / sec in a tunnel affects the ability to fly of the female of Aedes aegypti. So, apparently, even the wind speed can dramatically reduce mosquito activity and dengue transmission, in addition to climatic variables used in this study (KENNEDY, 1939).

Several works are being carried out in Brazil and worldwide, highlighting the use of the methodology of Box and Jenkins to predict dengue epidemy in Rio de Janeiro (LUZ ET. AL., 2008).

However, the relationship among several climatic factors and dengue information allow for early detection of epidemies, and thus to create effective strategies for the prevention of this disease (DEPRADINE AND LOVELL, 2004).

Moreover, it is necessary to imprve this type of study in other regions of Brazil due to climatic diversity that our country presents.

Conclusions

Through the analysis of time series, there was the influence of some climatic factors on the incidence of dengue.

In Cuiabá showed that the rain and the temperature has an influence on the maximum number of dengue cases while in SE, plus rain and maximum temperature, average temperature and humidity influenced.

Models adjusted for each regression city have in common the influence of maximum temperature and precipitation, and maximum temperature with a delay of four months in both models, and precipitation with a lag of three and five months to Cuiabá and two, three and four months late for Lavras.

Evaluating the coefficients of determination R ^{2}, which measures the proportion of variability of the observed values, compared with the adjusted values, we have the case of Cuiabá model to R ^{2} 0.31 and Lavras $R^2 = 0.68$.

In a second step, the city of Lavras, we consider only the series is also available for Cuiabá, the maximum temperature continued to influence the number of dengue cases with a delay of four months and precipitation with a lag of two, three and four months . However, the minimum temperature became significant at lags of five and six months. The R^2 was equal to 0.67, showing that although this new model to take into account information unless explains the number of dengue cases in SE as well as the first model.

We noted that with this type of approach has not been possible to propose a single model to explain the behavior of the number of dengue cases for the two cities. One reason for this failure may be strongly related to climate variability observed between the two cities chosen for analysis. Although adjusted models are different, both have a common component which is the influence of the maximum temperature with a delay of four months. This effect can be explained by the relationship of the biology of dengue, Aedes aegypti, and values of optimal temperature for its development. These temperatures are ideal for the development of vector ranges from 20^0 C 30^0 C.

Even observing the effect of temperature with a delay of 4 months in both models, precipitation was also significant, but with different time lags, but it is necessary for oviposition and hatching of larvae of mosquito presence of water. There is an urgent need to improve the monitoring and forecasting the incidence of dengue to reduce morbidity and mortality caused by this disease.

BICALHO, C.C.; SÁFADI, T.; CHARRET, I.C. A influência de fatores climáticos sobre epidemias de dengue nas cidades de Cuiabá (Mato Grosso) e Lavras (MG), Brasil, utilizando métodos estatísticos. *Rev. Bras. Biom.,* São Paulo, v.32, n.2, p.308-322, 2014.

- RESUMO: A dengue é um dos principais problemas de saúde pública no mundo. Estima-se que cerca de 2,5 bilhões de pessoas estão agora em risco de dengue. Diante deste contexto atual da doença desenvolvemos um modelo de série temporal na tentativa de identificar os fatores climáticos que contribuem para a proliferação da dengue nas cidades de Lavras (Minas Gerais) e Cuiabá (Mato Grosso) no Brasil. As séries para análise foram o número de casos notificados de dengue, séries de temperatura mínima, média e máxima, umidade relativa do ar e índice pluviométrico da cidade de Lavras e em Cuiabá consideramos as séries do número de casos notificados de dengue e séries de temperatura mínima e máxima e índice pluviométrico. Foram encontrados modelos que melhor se ajustam aos dados de acordo com a metodologia de Box e Jenkins e modelo de regressão que relaciona casos de dengue com fatores climáticos. Em Cuiabá, a precipitação e a temperatura máxima possuem influência no número de casos de dengue. Já em Lavras, além da precipitação e da temperatura máxima, também influenciaram o número de casos de dengue a temperatura média e a umidade. Os coeficientes de determinação R2, em Cuiabá e Lavras foram 0,31 e 0,68, respectivamente. No segundo ajuste para Lavras consideramos as séries de temperatura máxima e mínima e precipitação com um R2 de 0,67, e a temperatura máxima e a precipitação continuaram a influenciar no número de casos de dengue. Não foi possível propor um único modelo que explicasse o comportamento do número de casos de dengue para as duas cidades. Isto pode estar fortemente relacionado a variabilidade climática. Porém, ambos os modelos possuem um componente comum, que é a influência da temperatura máxima com defasagem de quatro meses.

- PALAVRAS-CHAVE: Séries temporais; dengue; clima.

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