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ANALYZING THE ASSOCIATION BETWEEN METEOROLOGICAL VARIABLES AND DENGUE-RELATED HOSPITALIZATIONS IN RIO BRANCO CITY/AC

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Resumo

O presente trabalho avalia a relação da precipitação, umidade relativa, temperaturas mínima e máxima do ar com a ocorrência de internações hospitalares por dengue no município de Rio Branco/AC, durante o período de 2008 a 2018. Os dados meteorológicos foram obtidos do Banco de Dados de Ensino e Pesquisa, pertencente ao Instituto Nacional de Meteorologia. Já a aquisição dos dados epidemiológicos, deu-se junto ao banco de dados do Departamento de Informática do Sistema Único de Saúde (DATASUS). A partir do teste de Mann Kendall, verificou-se tendência significativa decrescente nos casos de dengue. Em se tratando da correlação cruzada, a única variável que apresentou associação estatística com a dengue foi a umidade relativa, uma vez que durante todo o ano esta apresenta valores que são favoráveis para proliferação e longevidade do vetor. Os resultados mostram que as variáveis de precipitação e temperatura do ar podem subsidiar atividades específicas de prevenção e mitigação ao *Aedes Aegypti*.

Palavras-chave: Clima; Saúde; *Aedes Aegypti*.

ANALYSIS OF THE ASSOCIATION BETWEEN METEOROLOGICAL VARIABLES AND DENGUE HOSPITALIZATIONS IN RIO BRANCO CITY/AC

Abstract

The aim ofthe present study is to assess the correlation between rainfall, relative humidity, minimum and maximum air temperatures, and the incidence of dengue-related hospitalizations in Rio Branco City / AC, from 2008 to 2018. Meteorological data were collected in the Meteorological Database for Teaching and Research of the National Institute of Meteorology. On the other hand, epidemiological data were acquired from the database of the Unified Health System's Department of Informatics (DATASUS). Based on the Mann Kendall test, there was significant decreasing trend in the number of dengue cases. With respect to cross-correlation, relative humidity was the only variable presenting statistical association with dengue, since it often records values favorable for vector proliferation and longevity, throughout the year. Results have shown that variables such as rainfall and air temperature can support specific activities to prevent and mitigate the proliferation of *Aedes Aegypti.*

Keywords: Climate; Health; *Aedes Aegypti*.

ANÁLISIS DE LA ASOCIACIÓN ENTRE DIVERSAS ENFERMEDADES METEOROLÓGICAS E INTERNACIONALES DEL DENGUE EN LA CIUDAD DE RIO BRANCO / AC

Resumen

El presente trabajo evalúa la relación de la precipitación, la humedad relativa, las temperaturas mínimas y máximas del aire con la ocurrencia de hospitalizaciones por dengue en el municipio de Río Branco/AC, durante el período de 2008 a 2018. Los datos meteorológicos se obtuvieron de la Base de Datos de Enseñanza e Investigación, perteneciente al Instituto Nacional de Meteorología. La adquisición de datos epidemiológicos se obtuvo de la base de datos del Departamento de Informática del Sistema Único de Salud (DATASUS). La prueba de Mann Kendall mostró una tendencia significativa a la baja en los casos de dengue. En términos de correlación cruzada, la única variable que mostró asociación estadística con el dengue fue la humedad relativa, ya que a lo largo del año presenta valores favorables para la proliferación y longevidad del vector. Los resultados muestran que las variables de precipitación y temperatura del aire pueden subvencionar actividades específicas de prevención y mitigación del *Aedes Aegypti*.

Palabras-clave: Clima; Salud; *Aedes Aegypti*.

1. INTRODUCTION

The rate recorded for different vector diseases has been increasing on a yearly basis in tropical climate countries, such as Brazil, whose populations lack information, experience poor social and environmental conditions, and live under precarious sanitary conditions. Factors associated with climate change have been contributing to the high rate of diseases caused by vectors. (BARACHO, 2013). Dengue fever has epidemic potential, since this tropical disease presents the highest outspread rate (VIANA et al*.*, 2013).

The number of dengue case notifications in Brazil has significantly increased since the 1980s. Fast urbanization processes and unplanned cities, precarious living conditions, ineffective surveillance and vector control are some of the factors associated with dengue outspread. Dengue is a global concern, since trends head towards fast expansion in vector's geographic distribution and virus spread (FERREIRA et al., 2018).

Aedes Aegypti is a tropical and subtropical species mainly found between latitudes 35°S and 35°N, with rare incidence at latitudes close to 45°N, during Summer (FUNASA, 2001). It is pathologically described as acute systemic infection with viral etiology, which is transmitted by female *Aedes Aegypti* mosquitoes. Dengue is currently the most prevalent arbovirus in the world, since 40% of the global population is at risk of getting it (VIANA; IGNOTTI, 2013).

The incidence of this arbovirus is influenced by several factors, namely: climate change, population increase, urbanization, sanitary and socioeconomic conditions, among others (MENDONÇA et al*.*, 2009). It mainly affects tropical regions due to rainfall variation and increased air temperature rates, which are factors allowing the incubation and proliferation of the virus-transmitting mosquito (MONDINI et al*.*, 2009). Climate change affects the growth of 2 billion individuals susceptible to dengue. Simulations have suggested that by 2085, approximately 5 to 6 billion individuals (50% to 60% of the global population) may be at risk of disease transmission (HALES et al., 2002).

According to Neto et al. (2019), the socioeconomic issue of a given region has influence on the incidence of dengue because it does not provide adequate sanitation. Conseuently, the population is forced to use water-storage containers that can turn into breeding sites for *Aedes Aegypti*. Pará, Amazonas, Mato Grosso, Rondônia, and Acre states - which belong to the Amazonian region - experience this condition, since poor populations living in them, besides being subjected to the overall division into social classes, are also directly affected by annual bioclimatic seasonality during the rainy and dry seasons, - which are featured by floods, deforestation and wildfires. They also experience malaria and dengue outbreaks, and several respiratory diseases (DUARTE and MASCARENHAS, 2007).

Previous studies have shown seasonal pattern of dengue arbovirus incidence in Summer, due to higher rainfall and increased air temperature rates (ANDRADE, 2003; BARBOSA, 2007; SOUSA, 2005). Study conducted by Souza-Santos (1999) has shown significant association between the incidence of dengue cases and relative humidity; it has concluded that the highest mean number of positive *Aedes Aegypti* breeding sites was recorded in months when higher relative air humidity levels were observed.

Diagnoses carried out by Brazilian laboratories in 1981 and 1982 have confirmed 11,000 dengue cases in Boa Vista City, Roraima State (SCHATZMAYR, 2000). Nowadays, it is estimated that the arbovirus transmitted by the *Aedes Aegypti* mosquito has already reached all 27 federative units in the country, although not all municipalities have been affected by it (CONASS, 2019). At first, the meteorological and socioeconomic variations in the city appear to be aggravating factors for dengue development.

Studies about dengue have become increasingly relevant, not only for the health sector, but also for all sectors focused on supporting and strengthening the struggle to reduce risks associated with different diseases, as well as on improving the dialogue among sectors , operationalizing partnerships and sharing knowledge and experiencesto find solutions to different issues and to make the health system more effective (LOPES, 2015). The main aim of the current study was to investigate the association between meteorological conditions and dengue-related hospitalization cases in Rio Branco City, Acre State, from 2008 to 2018.

2. METHODOLOGY

2.1. Study site

Acre States is located in Southwestern Amazon region (07°07'S: 11°08'S; 66°30'W: 74°W); its territory covers 164,221.36 km², which corresponds to 4% of the Brazilian Amazon and to 2% of the national territory. Its territorial extension comprises 445 km to the North-South direction and 809 km between its East-West extremes. Acre shares international borders with Peru and Bolivia, as well as state borders with

Amazonas and Rondônia states. Its population comprises approximately 733,559 thousand inhabitants; 66% of these individuals are concentrated in urban areas (IBGE, 2010; ACRE, 2010).

Figure 1 - Geographic position of Acre State. Source: IBGE (2018).

Rio Branco City is the capital of Acre State; it is located in Western Amazon, at 152.5 m above sea level. It belongs to Vale do Acre mesoregion, Northeastern Acre State (9°30'S; 67°30'W: 69°30'W). The Eastern region of the state presents the most favored administrative infrastructure, health services and other relevant regional economy-related sectors (ACRE, 2010). The territorial extension of Rio Branco City covers 8,835.541 km², and it corresponds to 6.5% of Acre State's territory.

Table 1 - Most populous municipalities in Acre State. Source: IBGE (2019). Organization: the authors (2021).

Rank	Municipalities	Population (resident)	Area (Km²)
1°	Rio Branco	413.418	8.835,154
2°	Cruzeiro do Sul (AC)	78.507,00	8.779,391
3°	Sena Madureira (AC)	38.029,00	23.751,494
4°	Tarauacá (AC)	35.590,00	20.171,053
5°	Feijó (AC)	32.412,00	27.974,890

Climate in the city is classified as hot and humid equatorial with dry season (popularly called the Amazon summer) between June and September. According to the classification by Köppen (1948), the climate in the region is of the AM type; it presents monsoon rains, mean minimum temperature higher than 18ºC and short dry season, which does not significantly influence vegetation cover. According to Sousa (2019), mean annual rainfall rate in the region reaches 2,012 mm, whereas mean annual temperature reaches 25.46ºC and mean relative humidity is 87.4%.

2.2. Data and methods

Epidemiological data were collected at the databaseof the Unified Health System's Department of Informatics (DATASUS). Information about records of dengue-related hospitalizations (CID 10 - A90) derived from the Hospital Information System of the Unified Health System (SIH/SUS) - which is managed by the Ministry of Health, through the Department of Healthcare Services, in partnership with State and Municipal Health Secretariats - and processed by DATASUS of the Executive Secretariat of the Ministry of Health. Information available in DATASUS referred to the number of hospitalizations on a monthly basis, from 2008 to 2018.

In order to make the association between climate and health possible, it was necessary grouping data in the same time scale. Thus, monthly data about mean maximum temperature, rainfall and relative air humidity recorded by the reference meteorological station in Rio Branco City (n. 82915) were used in this process. They corresponded to the same period analyzed for hospitalization data (2008-2018). The complete historical data series are managed and made available by the Meteorological Database for Teaching and Research (BDMEP) of the National Institute of Meteorology (INMET). Thus, it was possible assessing the history of yearly dengue-related hospitalizations through Mann-Kendall test, as suggested by the World Meteorological Organization to observe trends in time series (MANN, 1945; KENDALL, 1975).

Mann-Kendall Test is a robust, sequential and non-parametric method used to determine whether a given data series presentstime trend susceptible to statistically significant changes. Another advantage of this method lies on the fact that it is little influenced by abrupt changes or non-homogeneous series (ZHANG et al., 2009).

The test statistics is given by the following equation (1):

$$s = \sum_{i=2}^{n} \sum_{j=1}^{i-1} sign\,(xi - xj) \quad (1)$$

Wherein the statistical variable S, for a series of n data subjected to Mann-Kendall test, is calculated based on the sum of signs (sgn) of the difference, pair by pair, among all values in the series (x_i) in relation to all initial and final values of the series (x_j). The sign ($x_i - x_j$) is equal to -1 for ($x_i - x_j$) < 0, 0 for ($x_i - x_j$) = 0, and 1 for ($x_i - x_j$) > 0.

Kendall (1975) has shown that S is normally distributed with mean E(S) and variance Var(S), which are calculated in contexts presenting equal x values, based on equation (2):

$$Var[S] = \frac{n(n-1)(2n+5) - \sum_{i-1}^{q}(tp-1)(2tp-5)}{18} \quad (2)$$

Wherein n is the number of observations, if the series has groups with equal observations; p is the number of groups with equal observations and ti is the number of data with equal values in a given group i (for example, a historical series presenting three values equal to each other would have 1 repetition of extension equal to 3, or ti =1 and i = 3). (LIRA, et al., 2020).

The parameterized statistical test (Z_{MK}) is computed by the following equation (3):

$$ZMK = \begin{cases} \frac{S-1}{\sqrt{Var[S]}} \\ 0 \\ \frac{S+1}{\sqrt{Var[S]}} \end{cases} \quad (3)$$

For S > 0; For S = 0; For S<0.

The incidence of statistically significant trend is evaluated based on the value of Z. This statistics is used to test the null hypothesis, i.e., there is no trend. Positive Z_{MK} value indicates increasing trend, whereas negative value indicates decreasing trend. In order to test the increasing or decreasing monotonic trend at p significance level, the null hypothesis is rejected if the absolute value of Z is higher than $Z_{1-p/2}$, based on the standard cumulative normal distribution table. The value of Z / 2, at 5% significance level, is 1.96. Positive values of Z indicate increasing trends, whereas negative values of it indicate decreasing trends (MENEZES; FERNANDES, 2016).

The association and response time between the investigated variables and the number of dengue-related hospitalizations in Rio Branco City were evaluated based on preliminary data analysis. The cross-correlation method was used for this purpose, since it measures similarity between signals of two variables, based on delay applied to one of them. This technique, which enables identifying the degree to which, and time when, the two variables are correlated to each other, reflects how the two processes correlate to each other (GOMES et al., 2018). Its graphical representation determines whether, and to what extent, a given data series leads to another series. The cross-correlation function estimator is calculated through the following equation (4):

$$\hat{\rho}xy\ (h) = \frac{\sum_{t=1}^{n-h}(xt+h-\bar{x})(yt-\bar{y})}{n^{-1}\sum_{n=1}^{n}(xt-\bar{x})^2(\sum_{t=1}^{n}yt-\bar{y})^2} \quad (4)$$

Wherein, $\boldsymbol{X_t}$ and $\boldsymbol{Y_t}$ are the time series; x and y are the means; h is the lag coefficient between the e series; and n is the number of observations. The statistical method was carried out in the R free statistical software, version 3.5.1.

3. RESULTS AND DISCUSSION

January to March was the lime lapse presenting the largest number ofmonthly records of dengue cases. It accounted for 60% of the total number of cases, with emphasis on February. As for the annual rates, 2009 and 2010 were the years mostly recording hospitalizations, since 65% of dengue cases were registered within this time interval.

Figure 2 shows the distribution of dengue-related hospitalizations from 2008 to 2018. The years of 2009, 2010 and 2011 recorded the highest hospitalization rates. There was notable decrease in the number of cases from 2012 onwards. Based on the Mann Kendall test, trends of decrease in the number of cases were statistically significant (p-value 000.1).

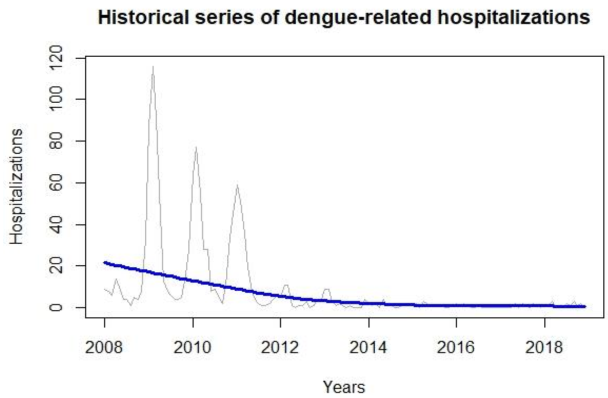

Figure 2 - Historical series of dengue-related hospitalizations and their respective trend. Source: SIH/SUS (2019). Organization: elaborated by the authors (2021).

Although recorded values have decreased, it did not mean that the disease was mitigated. The Notifiable Diseases Information System recorded approximately 72,000 disease notification cases from 2008 to 2018. The number of dengue-related hospitalizations has decreased since then, although the vector remains active (SINAN, 2019).

Mean rainfall rate recorded for the analyzed period (Figure 3) has evidenced the highest rainfall rate in January and the lowest rate in July. According to Baracho et al., (2014), rainfall influence on the disease is often significant, mainly in cases taking place in Summer, which presents intense rainfall index. January also stands out for presenting the highest rainfall variability, whereas higher outliers are often observed in February, June, September and November.

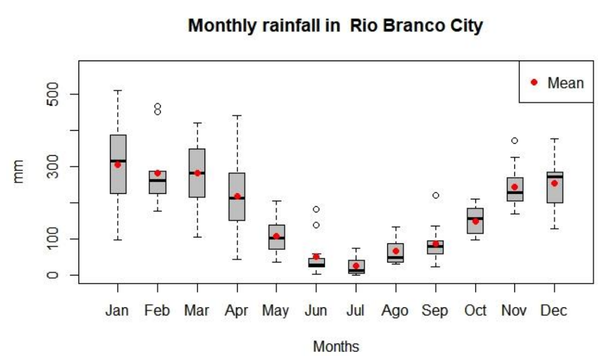

Figure 3 - Mean monthly rainfall recorded for Rio Branco City, from 2008 to 2018. Source: BDMEP/INMET (2019). Organization:elaborated by the authors (2021).

Temperature has direct influence on *Aedes Aegypti* mosquito cycle, which ranges from 5 to 7 days. Therefore, proper environmental conditions are necessary to enable its development. According to Pacheco et al (2017), the ideal temperature range for *Aedes Aegypti's* biological cycle goes from 22°C to 30°C. On the other hand, temperatures below the aforementioned ones increase the estimated time for the mosquito to develop.

Figures 4 and 5 present two graphs with mean maximum and minimum air temperatures. Based on Figure 4, the lowest temperature (31°C) was recorded in June, whereas the highest temperature was observed in September (34°C). Mean maximum temperature in the region has shown high variability from June to August; these months correspond to the transition from the lowest to highest temperature values.

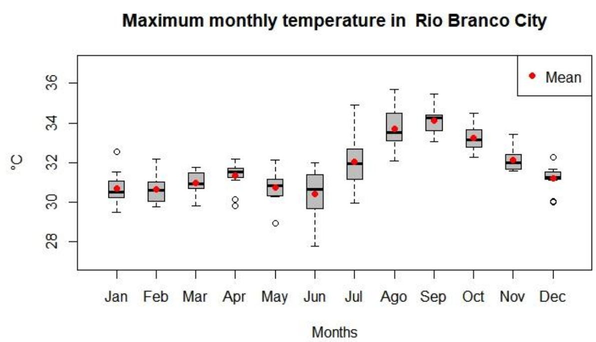

Figure 4 – Mean maximum monthly temperature in Rio Branco City, from 2008 to 2018. Source: BDMEP/INMET (2019). Organization: elaborated by the authors (2021).

Based on the comparison between the mean monthly maximum temperature and rainfall graphs (Figures 3 and 4), the months recording the highest mean maximum temperatures were the ones presenting the lowest rainfall rates. According to the mean monthly minimum temperature graph (Figure 5), the lowest temperature value was recorded in July, approximately 18º C, whereas the highest temperature was observed in November, approximately 24º C. It is important emphasizing that variability in minimum temperature values was lower than that observed for maximum temperature values. In addition, higher outliers were identified in January, July and September.

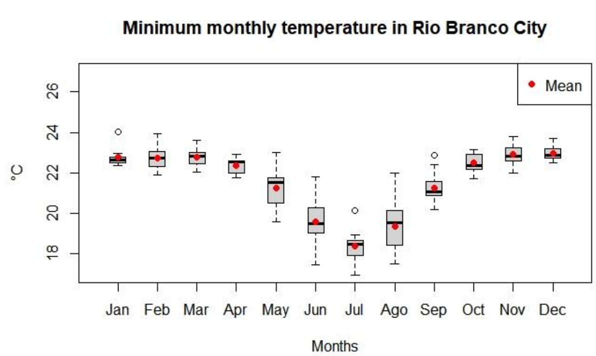

Figure 5 – Mean minimum monthly temperature in Rio Branco City, from 2008 to 2018. Source: BDMEP/INMET (2019). Organization: elaborated by the authors (2021).

According to Baracho et al (2014), mosquito species *Aedes Aegypti* has great potential to develop at relative air humidity ranging from 70% to 100%. This temperature range enables satisfactory development at all cycle stages. The analysis applied to monthly relative humidity (Figure 6) has shown high humidity rates: the lowest rate was recorded in August (74%), whereas the highest rate was observed in January (90%) - it enabled favorable mosquito proliferation conditions.

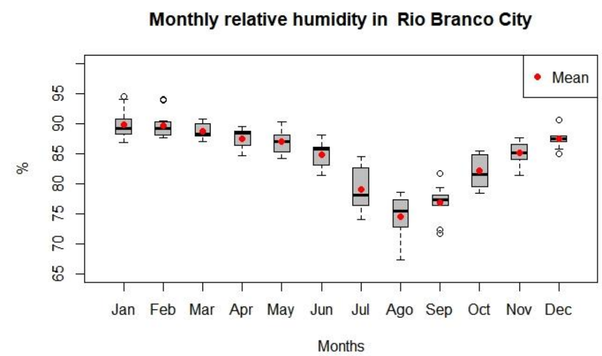

Figure 6 - Monthly relative humidity in Rio Branco City, from 2008 to 2018. Source: BDMEP/INMET (2019). Organization: elaborated by the authors (2021).

The chart of monthly hospitalization cases in the city (Figure 7) has shown dengue-related morbidity values. The number of hospitalization cases was larger from November to April, and it decreased from May to October. Months recording the highest hospitalizations rates were the ones presenting favorable atmospheric scenario for mosquito proliferation, such as increased rainfall and relative humidity rates, in association with milder mean air temperatures.

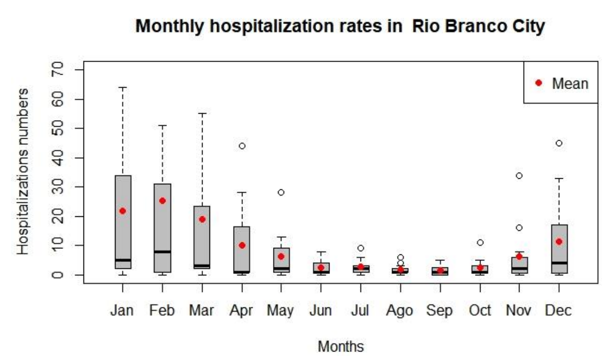

Figure 7 – Monthly hospitalization rates in Rio Branco City, from 2008 to 2018. Source: SIH/SUS (2019). Organization: elaborated by the authors (2021).

Viana et al. (2013) have also associated increased number of dengue cases with rainfall rate. However, according to Figures 3-7, significant meteorological factors associated with dengue transmission can change depending on the climate conditions in the analyzed region.

Months recording the highest rates of dengue cases were the ones when the temperature ranged from 30°C to 32°C, whose thresholds were higher than those suggested in the literature. This outcome suggests mosquito's adaptation in order to resist to higher temperatures, over the years. Moreover, dengue case rates have decreased in months when the temperature also decreased, a fact that evidenced direct association between these two variables. However, both Summer and Winter overall recorded high temperature rates, and they enabled favorable for vector proliferation conditions (FERREIRA et al., 2018). According to Pacheco et al. (2017), decreased number of dengue cases does not mean that the mosquito stopped reproducing.

Visual rainfall analysis has shown association between rainfall indices and dengue cases. The period from December to April, which held the months presenting high monthly rainfall rates, accounted for the largest monthly number of confirmed dengue cases at the investigated site. According to Baracho et al. (2014), it happened due to water accumulation in artificial containers kept in individuals' homes, since they end up becoming breeding sites for *Aedes Aegypti* mosquitos. Based on relative air humidity observations, it was possible seeing humidity peaks coinciding with dengue-related morbidity peaks in the population (Figure 6). The region presented high humidity rate throughout the year; the highest values were observed in months recording the highest disease incidence.

According to Ferreira et al. (2018), rainfall rates and high temperatures lead to increased number of breeding sites and dengue cases. On the other hand,dry periods and low temperatures lead to decreased number of vectors, although it is not enough to stop disease transmission, due to the hematophagic behavior presented by the vector throughout the year. Horta et al (2014) have shown that models based on climate variables that take into consideration the interval among rainfall, air temperature and dengue cases can be useful in dengue control programs implemented in tropical countries. In practical terms, the herein adopted cross-correlation technique has shown that using only rainfall and hospitalization data was not enough to enable investigating rainfall-dengue incidence association time (Figure 8).

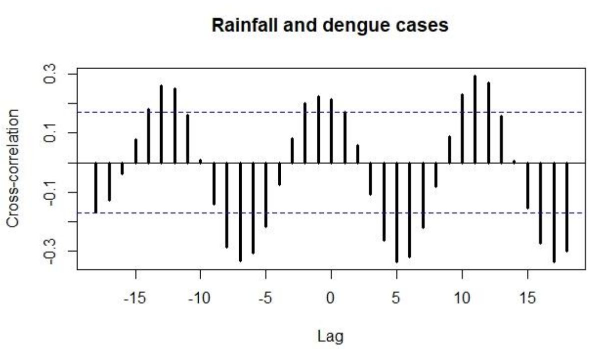

Figure 8 - Cross-correlation between rainfall and dengue cases in Rio Branco City, from 2008 to 2018. Source:SIH/SUS (2019); BDMEP/INMET (2019). Organization: the authors (2021).

It is possible seeing association between maximum temperature and dengue cases, which indicates that seasonality is fundamental to enable visualizing this correlation. Assumingly, mosquito proliferation contributes to the incidence of hospitalizations in the following period. This assumption can be confirmed thorugh Lag 7 in the cross-correlation between maximum air temperature and dengue cases (Figure 9).

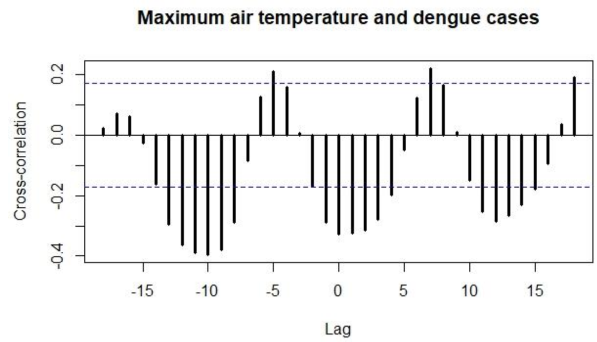

Figure 9 - Cross-correlation between maximum air temperature and dengue cases in Rio Branco City, from 2008 to 2018. Source:SIH/SUS (2019); BDMEP/INMET (2019). Organization: the authors (2021).

Minimum temperature has shown inverse association with lags 3, 4 and 5 in the cross-correlation between minimum temperature and dengue cases (Figure 10). This outcome has indicated that changes in minimum temperature contribute to decreased number of dengue hospitalizations, with lag of 3 to 5 months.

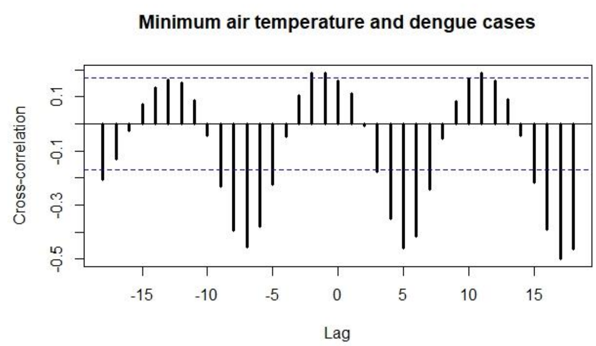

Figure 10 - Cross-correlation between minimum air temperature and dengue cases in Rio Branco City, from 2008 to 2018. Source: SIH/SUS (2019); BDMEP/INMET (2019). Organization: elaborated by the authors (2021).

Cross-correlation analysis (Figure 11) has shown prevalent seasonality sign between relative air humidity and dengue-related hospitalizations. Therefore, it is possible suggesting that the seasonal cycle of the meteorological variable had direct influence on hospitalization cases, based on significant associations between relative humidity and dengue-related hospitalizations observed over the investigated periods. These results corroborate the study by Ramalho (2008), who showed the influence of high relative humidity rate on feeding patterns, increased reproduction rate and on longer longevity of *Aedes Aegypti* specimens.

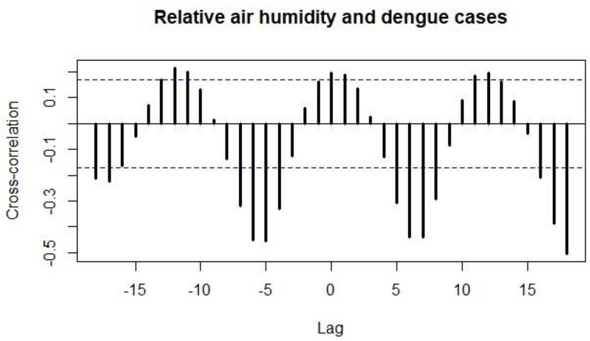

Figure 11 - Cross-correlation between relative air humidity and dengue cases in Rio Branco City, from 2008 to 2018. Source: SIH/SUS (2019); BDMEP/INMET (2019). Organization: elaborated by the authors (2021).

4. FINAL CONSIDERATIONS

Based on associations between meteorological variables and dengue-related hospitalization cases in Rio Branco City, from 2008 to 2018, the current study has statistically evaluated the correlation of variables such as rainfall, relative air humidity, minimum and maximum air tempe-rature to hospitalization cases registered at DATASUS.

Significant associations between meteorological variables and dengue-related hospitalization cases were observed in Rio Branco City, Acre State. The scenario was favorable for *Aedes Aegypti* reproduction under high rainfall and relative air humidity conditions, in association with milder temperatures. It is important highlighting the decrease observed in hospitalization records, which recorded significant downward trend in 61% of cases, from 2012 to 2018. However, it did not mean decrease in disease rates, since there is evidence of increased number of notifications recorded at SINAN, for the same period-of-time.

Although the herein performed evaluations have prioritized Rio Branco City (the place presenting the largest proliferation of *Aedes Aegypti* mosquitoes in Brazil), the current results corroborate with research previously carried out in other regions, which referred to atypical maximum air temperature values favorable for mosquito development, and whose thresholds ranged from 30° C to 32° C. In addition, the combination of meteorological variables such as rainfall and air temperature can be useful for dengue control programs implemented in tropical regions.

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