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## Major Article

# Climatic variables associated with dengue incidence in a city of the Western Brazilian Amazon region

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### Abstract

**Introduction:** This study aimed to examine the impact of climate variability on the incidence of dengue fever in the city of Rio Branco, Brazil. **Methods:** The association between the monthly incidence of dengue fever and climate variables such as precipitation, temperature, humidity, and the Acre River level was evaluated, using generalized autoregressive moving average models with negative binomial distribution. Multiple no-lag, 1-month lag, and 2-month lag models were tested. **Results:** The no-lag model showed that the incidence of dengue fever was associated with the monthly averages of the Acre River level (incidence rate ratio [IRR]: 1.09; 95% confidence interval [CI]: 1.02–1.17), compensated temperature (IRR: 1.54; 95% CI: 1.22–1.95), and maximum temperature (IRR: 0.68; 95% CI: 0.58–0.81). The 1-month lag model showed that the incidence of dengue fever was predicted by the monthly averages of total precipitation (IRR: 1.21; 95% CI: 1.06–1.39), minimum temperature (IRR: 1.54; 95% CI: 1.24–1.91), compensated relative humidity (IRR: 0.90; 95% CI: 0.82–0.99), and maximum temperature (IRR: 0.76; 95% CI: 0.59–0.97). The 2-month lag model showed that the incidence of dengue fever was predicted by the number of days with precipitation (IRR: 1.03; 95% CI: 1.00–1.06) and maximum temperature (IRR: 1.23; 95% CI: 1.05–1.44). **Conclusions:** Considering the impact of global climate change on the region, these findings can help to predict trends in dengue fever incidence.

**Keywords:** Dengue. Climate. Climate change. Amazonian ecosystem. Brazil.

## INTRODUCTION

Dengue fever is currently the most important arboviral disease in the world. It is endemic to over 100 countries, mainly located in tropical and subtropical regions[1-4]. In South America, the majority of cases occur in Brazil, with over 1.5 million reported cases in 2015, and an incidence rate of 763 per 100,000 inhabitants[5,6]. This disease is caused by four distinct viral serotypes, transmitted to humans by *Aedes aegypti* mosquitoes. Infestations by these mosquitoes have occurred in Brazil since 1979. Since then, epidemic outbreaks have been progressively reported in the country, where the four viral serotypes can be currently found[3,4,7]. Combating vectors is the main approach to controlling dengue fever and other diseases, such as Zika and Chikungunya, which are also transmitted by these mosquitoes[2,8].

The establishment and permanence of vectors in a specific environment have been associated with a variety of factors, including deforestation, disorganized urbanization, urban swelling, population displacement, lack of water and sanitation, climate variability, and environmental changes[5,9-12].

Brazil is a country with high climate and environmental variability in its regions; therefore, regional particularities can affect dengue fever transmission in different ways[1]. The Brazilian Amazon region, for example, covers an extensive forest area and natural ecosystems that offer favorable conditions for dengue fever[13,14]. However, there is limited research contributing to a better understanding of the phenomenon and allowing improvement in the health services.

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This study aimed to examine the association between the monthly incidence of dengue fever and environmental variables between 2001 and 2012 among the population of a city in the Western Brazilian Amazon region.

## METHODS

This work corresponds to an ecological study in which we analyzed the incidence of dengue cases reported to the surveillance system over a period of 12 years in an endemic city. The study was conducted in Rio Branco, the capital city of the state of Acre, located in the northern region of Brazil. According to a 2010 census, Rio Branco has a population of over 336,000 inhabitants[15]. In this region, the climate is hot and humid. Temperatures range between 25°C and 40°C throughout the year, except for a few days when the weather is cold, and temperatures are around 15°C. The monthly compensated relative humidity remains constantly high, ranging between 60% and 95% throughout the year[16]. The city is located on the banks of the Acre River, one of the main rivers of the state, which divides the city into two regions: the first and second districts. During the rainy periods, usually between October and April, the river level rises and most of the times exceeds the alert level for overflowing (13.5 meters), leaving a large part of the city flooded[17-19].

This study used data regarding the number of monthly cases of classical and hemorrhagic dengue fever derived from individuals living in the city of Rio Branco. Cases were recorded according to the month of onset of the first symptoms of the disease[20]. These included both suspected and laboratory-confirmed cases. Suspected cases, subsequently discarded after laboratory testing, were excluded. Data obtained between January 1, 2001 and December 31, 2012 were organized according to 11 age groups. Data were extracted from the Notifiable Diseases Information System from the Brazilian Public Health System (SINAN/SUS – Sistema de Informação de Agravos de Notificação/Sistema Único de Saúde), available on the DATASUS website (SUS Department of Informatics, maintained by the Brazilian Ministry of Health)[20]. For the analyses, the monthly incidence of dengue fever was calculated for every 100,000 inhabitants. These incidences were calculated according to year, month, and age group. Estimates of population size were obtained from the Brazilian Institute of Geography and Statistics (IBGE - *Fundação Instituto Brasileiro de Geografia e Estatística*)[21].

The following environmental variables, particularly climate variables, were used: number of days with precipitation per month, monthly average total precipitation (in millimeters), monthly average maximum temperature, compensated and minimum average temperature (in degrees Celsius), and monthly average compensated relative humidity (as a percentage). These data were extracted from the information bank available on the website of the National Institute of Meteorology (INMET - Instituto Nacional de Meteorologia)[22]. The only environmental variable that was not a climate variable was the monthly average of the Acre River level (in meters), obtained from the hydrological information system, available on the National Water Agency (ANA - Agência Nacional das Águas) website[23]. This variable was considered because of its strong association with climate variability.

The statistical associations between the monthly incidence of dengue fever and the monthly average of climate and environmental variables were evaluated using the generalized autoregressive moving average (GARMA) models with a negative binomial distribution and logarithmic link function[24]. These models have been increasingly used in time-series studies, as they allow modeling of the existing serial correlations among the data[25-28].

To evaluate the best order of the GARMA model, several models with different orders were compared using the Akaike information criterion (AIC), based on the selection of the model with the shortest information distance from the true model and, therefore, with the lowest AIC[29]. Variables were selected according to the backward method, removing the variable with the greater p-value at each step, until only significant variables remained in the model ($p < 0.05$)[30].

These models tested the association between the monthly incidence of dengue fever and environmental variables, such as the averages of climate variables, and the monthly average of the Acre River level in the same month. Three models including independent variables were developed: the no-lag model, the 1-month lag model (1 month earlier), and the 2-month lag model (2 months earlier). These lag models are justified because the effect of the environmental variables on the incidence of dengue fever may require an induction period of many weeks. Specifically, induction can involve several processes, such as formation of breeding sites, development of vectors, transmission processes, incubation period, and time until diagnosis and notification of the disease[2-4,11].

There were 21 missing pieces of information on the dengue fever variables (1.32% of total data), distributed across all age groups. These data were imputed using the expectation maximization algorithm method[31]. All data from this research were obtained from secondary sources with free access, so approval by the Research Ethics Committee was not needed.

## RESULTS

### General descriptive analysis

Over the course of 12 years, the Epidemiological Surveillance sector of the Municipal Health Department of Rio Branco reported 81,124 cases of dengue fever. The highest incidence of the disease occurred in 2010 with 9,792.3 cases per 100,000 inhabitants, followed by 2009 with 5,669.5 cases and 2011 with 4,983.9 cases per 100,000 inhabitants (**Figure 1**).

The highest monthly average incidence of dengue fever per 100,000 inhabitants during the study period occurred between October and April, corresponding to the rainy season in the region (**Figure 2**).

The highest average incidence of dengue fever per 100,000 inhabitants between 2001 and 2012, in the city of Rio Branco, occurred in older people between 60 and 69 years, followed by adults between 40 and 59 years. A higher incidence was also observed among older people over 70 years of age (**Figure 3**).

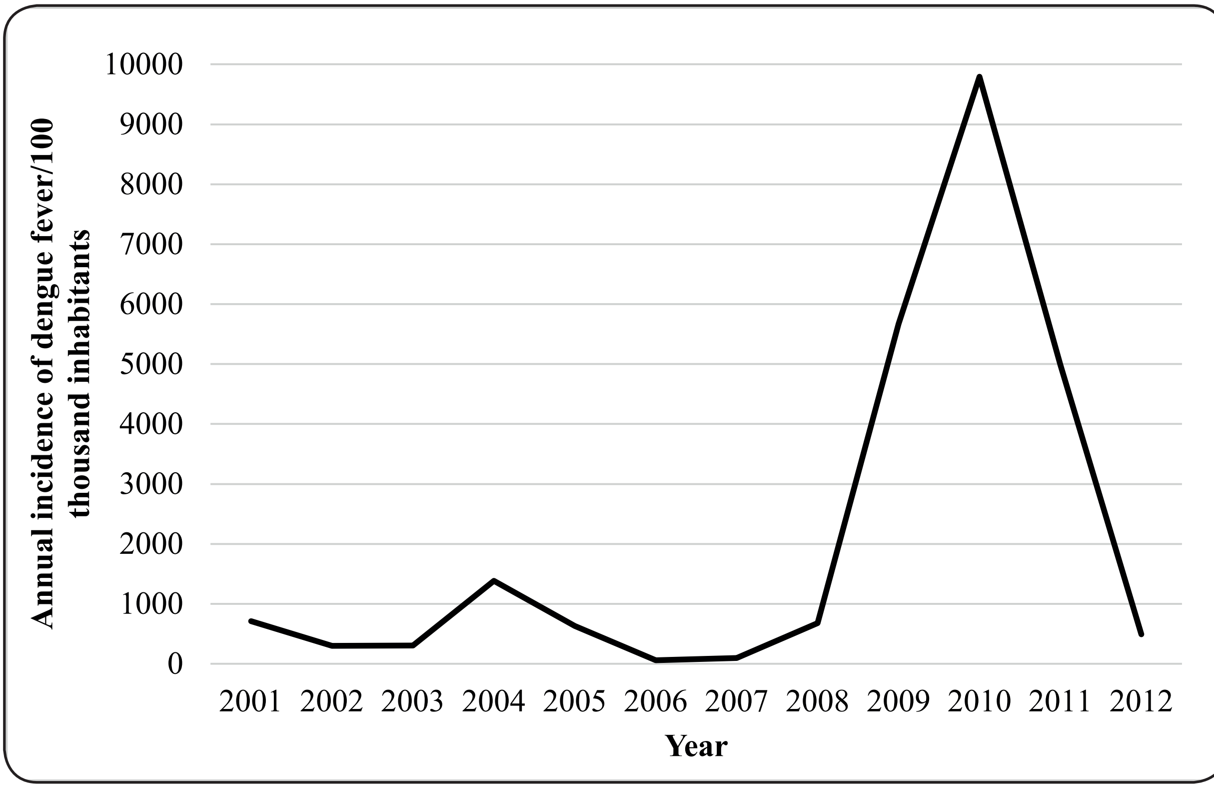


**FIGURE 1:** Annual incidence of dengue fever between 2001 and 2012 in Rio Branco, Brazil.

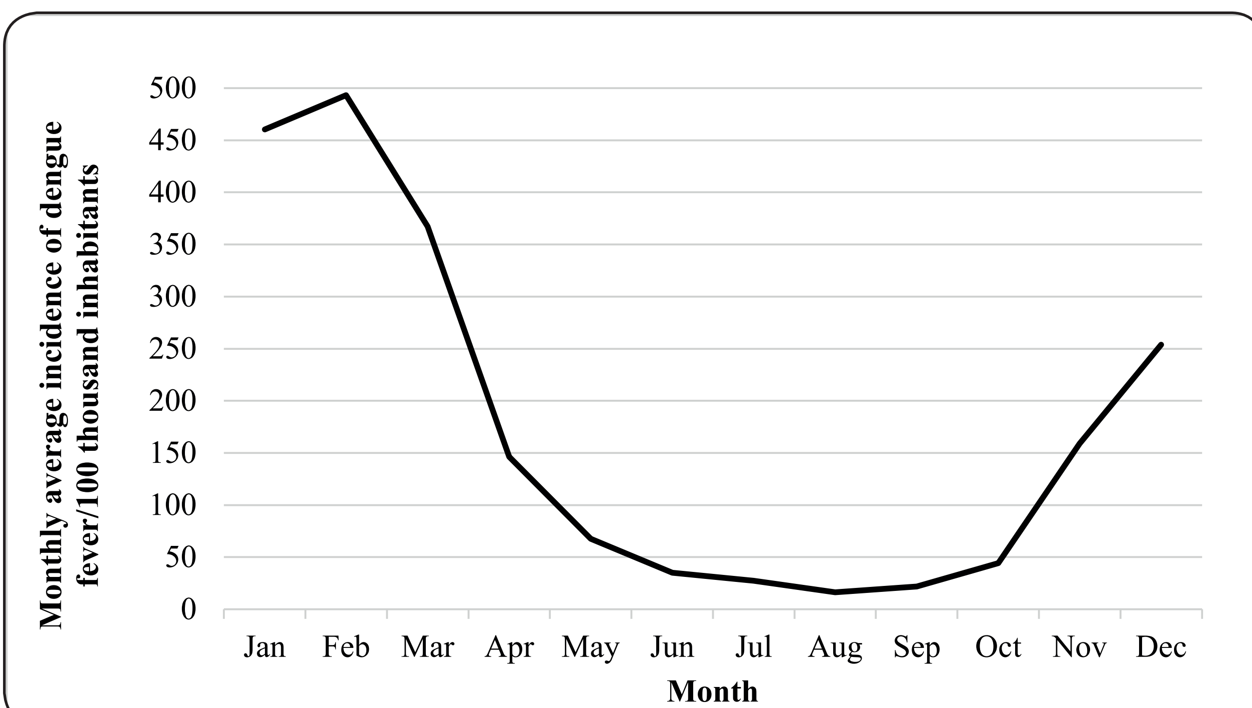


**FIGURE 2:** Monthly average incidence of dengue fever between 2001 and 2012 in Rio Branco, Brazil.

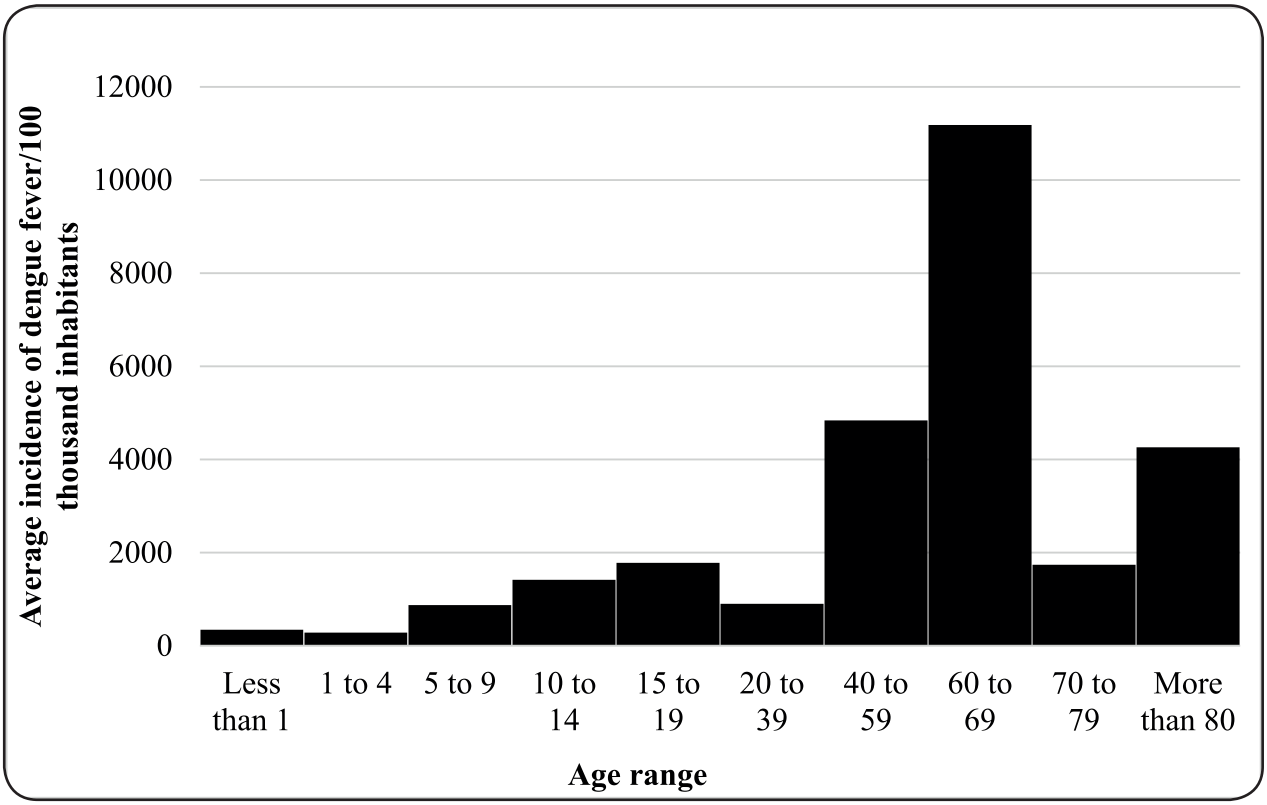


**FIGURE 3:** Average incidence of dengue fever according to age range in Rio Branco, Brazil, 2001-2012.

### Inferential analysis

GARMA models with a binomial distribution with distinct orders were adjusted for each of the analyses. The following variables were selected in these models: monthly average of the Acre River level, number of days with precipitation per month, monthly average total precipitation, monthly average of average compensated relative humidity, and monthly averages of minimum, compensated, and maximum temperatures (**Table 1**).

In the no-lag model (**Table 1**), each meter increase in the Acre River level was associated with a 9% increase in the monthly incidence of dengue fever (incidence rate ratio [IRR]: 1.09; 95% confidence interval [CI]: 1.02–1.17). Each 1°C increase in the monthly average compensated temperature was associated with a 54% increase in the monthly incidence of the disease (IRR: 1.54; 95% CI: 1.22–1.95). However, for each 1°C increase in the monthly average of maximum temperature, there was an associated 32% decrease in the monthly incidence of dengue fever (IRR: 0.68; 95% CI: 0.58–0.81).

The 1-month lag model showed that each millimeter increase in the monthly average of total precipitation was associated with a 21% increase in the incidence of dengue fever in the following month (IRR: 1.21; 95% CI: 1.06–1.39). In the same model, each 1°C increase in the monthly average minimum temperature predicted a 54% increase in the monthly incidence of the disease (IRR: 1.54; 95% CI: 1.24–1.91). Relative humidity and maximum temperature appeared to have a negative effect on the incidence of dengue fever (**Table 1**). Specifically, a 1% increase in the monthly average compensated relative humidity was associated with a 10% decrease in the incidence of dengue fever in the following month (IRR: 0.90; 95% CI: 0.82–0.99). Each 1°C increase in the monthly average maximum temperature predicted a decrease of approximately 24% in the monthly incidence of dengue fever (IRR: 0.76; 95% CI: 0.59–0.97).

In the 2-month lag model, the number of days with precipitation and the maximum temperature were significantly associated with the subsequent incidence of dengue fever. Each additional day of precipitation per month was associated with a 3% increase in the incidence of the disease (IRR: 1.03, 95% CI: 1.00–1.06). Furthermore, each 1°C increase in the monthly average compensated temperature was associated with a 23% increase in the incidence of dengue fever (IRR: 1.23; 95% CI: 1.05–1.44).

The autoregressive (φ) and moving average (θ) parameters for each of the models were significantly different from zero, justifying the selection of the GARMA model order. The dispersion parameters (σ) were also significantly different from zero, which confirms the assumed dispersion of the negative binomial model.

## DISCUSSION

The results of this study show that a variety of environmental variables, particularly those related to climate variability, can be indicative or predictive of the incidence of dengue fever in

**TABLE 1:** **Association between the variables, using GARMA models (Rio Branco, Brazil, 2001-2012).**

| | No-lag model | 1-Month lag model | 2-Month lag model |
|---|---|---|---|
| **Inferential analysis** | | | |
| **Variable** | **IRR (95% CI) p-value** | **IRR (95% CI) p-value** | **IRR (95% CI) p-value** |
| Acre River level | 1.09 (1.02–1.17) 0.01 | - | - |
| No. of days with precipitation | - | - | 1.03 (1.00–1.06) 0.02 |
| Total precipitation | - | 1.21 (1.06–1.39) 0.004 | - |
| Relative humidity | - | 0.90 (0.82–0.99) 0.02 | - |
| Minimum temperature | - | 1.54 (1.24–1.91) <0.001 | - |
| Compensated temperature | 1.54 (1.22–1.95) <0.001 | - | 1.23 (1.05–1.44) 0.009 |
| Maximum temperature | 0.68 (0.58–0.81) <0.001 | 0.76 (0.59–0.97) 0.02 | - |
| **Model parameters** | | | |
| $\Phi^a$ | 0.59 (p < 0.001) | 0.60 (p < 0.001) | 0.60 (p < 0.001) |
| $\Theta^b$ | 0.30 (p = 0.002) | 0.32 (p < 0.001) | 0.44 (p < 0.001) |
| $\Sigma^c$ | 0.45 (p < 0.001) | 0.45 (p < 0.001) | 0.52 (p < 0.001) |
| **AIC** | | | |
| Lowest value | 1573.05 | 1560.38 | 1570.11 |

**GARMA:** generalized autoregressive moving average; **IRR:** incidence rate ratio; **CI:** confidence interval; **AIC:** Akaike information criterion. [a]Autoregressive parameters; [b]Moving average parameters; [c]Dispersion parameters.

Rio Branco. The association of the Acre River level with the increased incidence of dengue fever can be explained by the seasonal overflow of the river and floods in the region. Almost every year, during the rainiest months, the river exceeds its overflow level and floods most of the city[18,19,32]. The consequent increase in the number of available mosquito breeding sites on the streets favors the development of the vector in its egg, larva, and pupa phases, which occur in aquatic environments[7,33-35].

For the same reason, rainfall has also been highly associated with the occurrence of dengue fever[1,3,4,7,9-11]. In this study, both the days with precipitation per month (2-month lag model) and the monthly average of total precipitation (1-month lag model) were associated with an increased monthly incidence of dengue fever. Lags between climate variations and incidence of cases could be explained by the time required from breeding site formation to the diagnosis of the disease. The development of *Aedes aegypti* eggs to the adult phase requires approximately 2–3 weeks, depending on climate and environmental conditions. The incubation period in the host should also be considered and lasts approximately 1 week or slightly longer[10,11].

Temperature variation has also been associated with the magnitude and seasonality of dengue fever transmission. In Brazil, dengue fever outbreaks are typically observed during hot periods, usually at the end of summer[1,4,9,36]. This study found that increases in the monthly average minimum temperature, normally approximating 21°C, and in the average compensated temperatures, generally approximating 25ºC[16], were significantly associated with an increase in the incidence of dengue fever. This occurs because these temperatures are close to temperatures considered ideal for the development of dengue mosquitoes (between 22°C and 26°C)[37]. These temperatures favor the different phases of the vector development cycle, including maturation, survival, and population increase. They also favor hematophagic activity and viral replication in the vector[37-41]. Therefore, the incidence of dengue fever may be influenced by temperature increases that occurred up to 2 months earlier. Temperatures below 17°C are considered unfavorable for the feeding of the mosquito and result in slower development of the virus in the vector[42,43].

Our results also showed that, in this region, the effect of increasing the maximum temperature, approximately 32°C on average[16], seems to disadvantage the dynamics of dengue fever transmission. Most studies examining the association between temperature and occurrence of dengue fever have focused on temperatures that are close to or lower than the temperature considered optimal for the vector[37-43]. The literature lacks studies investigating higher temperatures (above 30°C). The results of our study suggest that temperatures above 32°C are much higher than the temperatures considered ideal for the vector. These temperatures also accelerate the evaporation and drying process of wastewater spread throughout the city, which would otherwise become a breeding site for the mosquito.

Interestingly, average relative humidity was negatively associated with dengue fever incidence. This conflicts with most studies reporting a positive correlation between these variables[44-46]. However, the particularities of each region's climate must be considered. For example, in Rio Branco, during the study period, the lowest value obtained for relative humidity was 67.25%, showing limited variation[16]. Therefore, this result could have been obtained owing to the climate of the region, which is quite hot and humid throughout the year, even in the months with the lowest dengue fever incidence (June to September).

Regarding the characteristics of the patients, the results of this study corroborate those reported in the South American literature, showing that the incidence of dengue fever is usually higher among adults and the elderly[4,47-50]. When dengue fever occurs in regions where virus circulation occurred relatively recently, the risk of developing the disease reaches its highest point in adults. This contrasts with observations in other endemic regions, such as Southeast Asia, where the force of infection is amplified and reaches its maximum strength at earlier ages[51].

However, in some Latin American countries and regions of Brazil, the average age of patients with hemorrhagic dengue fever is decreasing, and an increasing proportion of children are being affected[4,36,52]. This has mainly occurred after decades of disease permanence in the region and has been related to the progression of dengue fever viral serotypes and population immunity.

During the study period, dengue fever epidemics in Rio Branco occurred in 2009, 2010, and 2011, several years after the appearance of the first cases in the city. It appears that the local climate and ecosystem are favorable to the permanence and maintenance of the disease[7,10]. In the Brazilian Amazon, climate variability is intense, floods are frequent, and the process of urban occupation has occurred in an accelerated and precarious manner[53,54]. In addition, the increase in migration in recent decades has created environments with high population density and precarious social, economic, and infrastructure conditions[4,53-55]. In the city of Rio Branco, for example, a large part of the population lives in wetlands on the banks of the Acre River[56]. Furthermore, the low efficacy of control measures and the absence of specific effective interventions predict the permanence and propagation of arboviruses in the region[7,10,57].

In this context, the results presented are particularly important when confronted with the perspective of global climate change. There is a prospect of future temperature increases in the Amazon rainforest region, which may influence vector development and dengue fever transmission dynamics[58,59]. This increase in temperature can also influence the rainfall regime and the occurrence of floods in the region due to the warming of the tropical South Atlantic Ocean surface[60-62]. Climate change may affect the population according to social vulnerability. Therefore, studies contributing to the development of a greater understanding of the association between climate, environment, and health at the regional level can help to cope with the impact of climate change by encouraging relevant adaptive actions[3,33,58].

Studies based on secondary data, although providing valuable information for the investigation of environmental variables and their effects in the general population, are subject to significant limitations. We highlight the potential variations in the quality of the data collected and recorded over time, which may produce errors in the results. In this sense, it was not possible to evaluate the effects of the changes in the surveillance and health services, the greater access to diagnosis, and the increase in the number of diagnostic tests, which may have contributed to the notable increase in the reported incidence of the disease, largely observed during the last years of the study.

Conversely, while possible socioeconomic and demographic changes could have influenced the occurrence of dengue fever, these variables were not considered because serial measurements were not available. However, we postulate that socioeconomic and demographic variables would not explain the identified associations, as it is likely that these would remain relatively stable as opposed to the clear changes in the environmental and epidemiological variables analyzed in this study.

Although ecological studies have limitations in establishing inferences regarding individual risk factors, they are adequate to evaluate the effect of environmental determinants on health events. In that sense, this study identified climatic variables that can influence the incidence of dengue fever in this region. It should also be noted that, in addition to climatic variables, other variables may be involved in the dynamics of disease transmission, such as the circulation of different serotypes, the time of endemicity affecting the distribution of susceptible groups, and demographic density. In addition, underreporting of cases, which occurs primarily with less severe cases, may affect outcomes[50]. Nevertheless, these results can contribute to better planning and future decision-making aimed at preventing and mitigating the impact of the environment on population health. It would be useful to conduct complementary studies examining issues associated with socio-environmental vulnerability in different geographic areas of the region.

Most dengue fever cases worldwide have been recorded in Brazil. It is likely that this number will continue to increase for a long time, considering the prevalence of favorable factors for the maintenance of the disease in the country. These determinants are particularly evident in the Amazon region, which is characterized by rapid urbanization and social vulnerability. The results of this study show that these factors include climate variables such as precipitation and temperature.

The significant increase in the incidence of dengue was quantified for the first time in this study according to each additional meter in the river level, each additional day of rain in the month, each additional millimeter in the average total monthly precipitation, and each additional degree Celsius in the minimum and compensated average temperatures. These results highlight the intensity of the association between dengue incidence and climate variability in the city of Rio Branco. This information can be useful in the implementation of strategies to adapt to global climate change aimed at large cities in the Amazon region, where there is a high risk of a severe impact of climate change.

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**Conflict of Interest:** The authors declare that there is no conflict of interest.

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