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# DENGUE IN CHILDREN UNDER 15 YEARS: CLINICAL AND EPIDEMIOLOGICAL ASPECTS, STATE OF PARANÁ, IN THE PERIOD OF 2019 AND 2020

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**Abstract:** Dengue is an infectious viral disease, endemic in several regions of Brazil. Since the introduction of the virus in the country, young adults have been the most affected by the disease. However, in recent decades there has been an increase in cases in children. In view of this new scenario, a descriptive, retrospective observational study was carried out, with data from SINAN, which compared the incidence rate of dengue in children under 15 years of age, using the chi-square test, between age groups (under 1, 1 to 4, 5 to 9 and 10 to 14 years), also between genders and between reporting municipalities in Paraná in 2019 and 2020. The monthly distribution and association of the variables fever, leukopenia, presence of petechiae, test of the positive tie and serotype with the age range. Among the findings, May 2019 and March 2020 were the months with the highest rates of each year, with children under 1 year of age being the most affected. Fever was also more present in this group. There was no association of the disease with gender. The most prevalent serotype was DENV-2. Juranda, Inajá and Sertanópolis (14553, 13205 and 13072 cases per 100,000 inhabitants, respectively) were the cities with the highest incidence. Thus, it is expected to contribute to the clinical and epidemiological data of dengue in Paraná, since the disease in this particularly vulnerable population has increased considerably in recent years.
**Keywords**: *Aedes*. Dengue Fever. Spatial distribution. Epidemiological Survey.

## INTRODUCTION

Dengue is a disease that has a viral etiology, being transmitted by the bite of female mosquitoes of the Aedes aegypti species infected by the DENV virus. The virus has 4 different serotypes (DENV 1, DENV 2, DENV 3 and DENV 4) and belongs to the genus *Flavivirus*. It has a higher incidence in developing countries, as well as in tropical and subtropical regions - the hot and humid climate, precarious basic sanitation, associated with the urbanization process itself, favor the increase in cases. The disease has increased significantly in recent years, as almost half of the world's population lives in areas at risk of contamination. In this sense, due to the high morbidity, mortality and economic costs, this disease is considered an important public health issue (HARAPAN, 2020).

According to the Pan American Health Organization (PAHO), more than 1.6 million cases of dengue were registered in the Americas in the first 5 months of 2020, and about 65% of these were registered in Brazil. In the country, since the introduction of the virus during the 1980s, young adults have been the most affected by dengue; however, since 2006, there has been an increase in the number of cases, severity and need for hospitalization in children (BRASIL, 2009).

In 2019, 1,439,471 cases of the disease were reported in Brazil, which corresponds to 690 cases per thousand inhabitants (Epidemiological Bulletin, 2019). Between 2014 and 2019, the Midwest region led in number of dengue episodes, followed by the Southeast region. Regarding the serotype, between 2014-2017 the one that most affected Brazilians was DENV 1, and from 2017 it became DENV 2 (ONEDA, 2021).

Paraná presented the first cases of dengue in 1991, and in 1995 there was the first epidemic in the State, and today it leads in number of occurrences in the South region (PARANÁ, 2020). It is a notifiable disease, where notification must take place in the face of a suspected or confirmed condition, preventing the virus from circulating and reducing the number of cases, as blocking measures are adopted to contain the contamination of other individuals (MARQUES, 2020).

Regarding clinical manifestations, dengue varies in nature and severity, being

influenced by age, immunological and genetic characteristics of the patient, in addition to serotypes of the infecting virus (HALSTEAD, 2019). It presents from an asymptomatic or mildly symptomatic condition, to undifferentiated fever, dengue hemorrhagic fever or dengue shock syndrome (BIGARAN, 2021). In adults, it develops with high fever of sudden onset, accompanied by headache, retroorbital pain, myalgia, arthralgia, and gastric symptoms such as nausea, vomiting, lack of appetite and diarrhea. It can also manifest dermatological symptoms such as maculopapular rash, which may or may not be accompanied by pruritus. In most cases, it presents as a self-limiting disease with low mortality (BIGARAN, 2021). However, severe forms with hemorrhagic manifestations and shock may occur (AMORIM, 2021). Children, on the other hand, usually present a classic viral febrile syndrome, or even present with nonspecific symptoms such as drowsiness, apathy, food refusal, vomiting and diarrhea (RODRIGUES, 2015). In children under two years of age, symptoms such as headache, myalgia and arthralgia may be manifested by persistent crying and irritability (XAVIER, 2014).

Knowledge of the spatial distribution, clinical and epidemiological profile of the disease in children is essential, helping not only in the diagnosis and proper management of each case, as well as in a possible minimization of complications and death (PONE, 2015). According to Roque (2015), it is relevant in decision-making regarding the elaboration of health actions and a differentiated approach in places that present high risk.

So far, there are few studies with epidemiological data on dengue in children in Brazil. In this context, the present study aims to present clinical and epidemiological aspects of dengue in this age group in Paraná, as well as its geographic distribution in the State.

## METHODOLOGY

This is a descriptive, retrospective, observational study with a quantitative approach, of the occurrence and distribution of dengue cases in the population aged 0 to 14 years in Paraná.

Secondary data, in the form of microdata, from the Information System for Notifiable Diseases (SINAN) obtained through the Database of the Unified Health System (DATASUS) of individuals aged 0 to 14 years on the date of notification, who contracted dengue were used. in the period from 2019 to 2020 in Paraná. This group was divided into age groups: under 1 year old, 1 to 4 years old, 5 to 9 years old and 10 to 14 years old. Individuals with comorbidities and those who had the diagnostic hypothesis ruled out by serology were excluded. To calculate the incidences, population data estimated by the Ministry of Health/SVS/DASNT/CGIAE and SINASC were used and the result was multiplied by 100,000 inhabitants

$$\text{Incidence of cases} = \frac{\text{Total of occurrences}}{\text{Total of population}} 100.000$$

As independent variables, age, gender and municipality of notification were considered. The condition of dependent variable was attributed to serotype, date of notification, fever, snare test, leukopenia and presence of petechiae.

The date of notification was considered as the time of infection. The incidence of serotypes identified in each age group in the years 2019 and 2020 was calculated. To do so, the number of dengue cases in each age group was divided by the estimated population of children corresponding to the period and multiplied by 100,000. Likewise, the coefficient of incidence of Dengue was calculated by age group, as well as the coefficient of incidence

of fever, lasso test, leukopenia and petechiae in cases of Dengue, also by age group. In addition, three general Dengue incidence rates were obtained in individuals aged up to 14 years, per 100,000 inhabitants: one from 2019, another from 2020, and the average incidence for the entire period. The monthly average number of cases was also calculated. For geographic distribution, the incidence rate per municipality was considered separately in 2019 and 2020.

Graphics and data analysis were performed using the R software (version 4.1.1), as well as regional heat maps and Chi-Square association tests. Pearson's chi-square test is valid in cases where the two variables are categorical and is capable of assessing the association between these qualitative variables. The basic principle is to compare proportions, identifying whether there is greater or lesser recurrence at a given level of a factor. The hypotheses to be tested are:

H0: There is no association between the variables;

H1: There is an association between the variables.

The regional heat maps are generated via the "spdep" package, and are based on the incidence of cases in each region, assigning darker colors to regions with higher incidence and lighter colors to regions with lower case rates (BIVAND, 2018 ).

## RESULTS AND DISCUSSION

An initial sample of 76044 reported cases of dengue was obtained in individuals aged up to 14 years, without comorbidities (23563 and 52481 in 2019 and 2020, respectively), with a statistically significant difference (= 475.82; p-value < 0.0001) between years. Thus, the result found for infantile dengue, dialogues with the data found for the disease at all ages in the analyzed period (PARANÁ, 2021).

In 2020, the country faced the onset of the COVID-19 pandemic; according to Mascarenhas (2020), during this period, Brazil was ahead of the number of dengue cases, when compared to the weeks of the period between 2015 and 2019, before the onset of the pandemic in the country. However, in the weeks following the spread of the coronavirus in the country, the epidemiological data of dengue decreased. Thus, despite the statistical analyzes of this study showing that the year 2020 showed more alarming numbers in relation to cases, these values could be even higher given the hypothesis of underreporting of the disease in this year.

When analyzing the incidence rate of dengue by age group (Figure 1), children under 1 year old were the most affected both in 2019 (1327 cases per 100 thousand inhabitants) and in 2020 (3021 cases per 100 thousand inhabitants), despite the age group of 10 to 14 years presented more notifications in absolute values (Figure 2). It was found that a child aged less than 1 year is twice as likely to have the disease compared to a group of children aged 1 to 4 years (Table 1). Two factors can justify this finding: most repellents are contraindicated for children younger than 6 months, and for those older than 6 months to 2 years, prolonged use of any repellents is not indicated (BASQUES, 2018); and the younger the child, the greater the inability to defend themselves directly against the mosquito, leading to greater vulnerability of this age group to insect bites. In the study on the prevalence of dengue in Brazil, Menezes (2021) highlights a greater involvement of individuals aged 20 to 39 years, which corresponds to 38% of cases between the years 2010 and 2019.

Dengue is considered a public health problem for countries in tropical and subtropical areas. The World Health Organization (WHO) points out that more than 2.5 billion people, that is, almost 40%

of the world's population, live in areas at high risk for the occurrence of the disease (MULIK, 2021). Vilches (2013) and Ribeiro (2006) discuss the seasonal effect of dengue, with peaks occurring in some months of the year and remission of cases in others, demonstrating a certain periodicity in the occurrence of the disease according to the variation in temperature and temperature. rainfall, favoring or preventing conditions for the development of the mosquito. In this work, it was found that the peak in the average number of dengue cases between the two years (Figure 3) occurred in March, with more than 8,750 cases of dengue in children in Paraná. And, when considering the monthly distribution (Figure 4), April and May 2019 and February and March 2020 had the highest rates, with a statistically significant difference between years (= 61691.03; p-value < 0.0001). August had the lowest average number of notified cases in the period considered. According to Loureiro (2021), the study carried out in Alto Paraíso-PR, on the number of reported dengue cases from 2011 to 2020, the months with the highest number of cases during the evaluated time interval were March and April. Thus, the author's study, despite being related to a specific city in the State of Paraná, obtained similar results to this study.

In the analysis of association tests applied to the variables age, gender, fever (for each age group), serotype and year (Table1), it is possible to verify that only gender did not present a statistically significant association with the diagnosis of dengue in children. This result is also found in the epidemiological study by Lima (2019) in Maringá. However, this result contrasts with that of a study with adults on the number of dengue cases in Brazil between 2010 and 2019, which revealed a predominance of dengue occurrence in the female population, representing 55.7% (MENEZES, 2021).

The introduction of dengue in Brazil was due to serotypes 2 and 4 in the 1980s, with DENV-2 being the cause of hemorrhagic dengue in 1990, registered in Rio de Janeiro. The introduction of DENV-3 occurred in the 2000s. As serotypes advanced and were introduced, there was a worsening in severe cases and a greater prevalence of the disease in the pediatric population (ABE et al, 2012.). In this work, only 1.34% of the serotypes (1020 of 76044) were identified. Of these, DENV-2 has the highest incidence rate (= 87.24; p-value < 0.0001) in all age groups when looking at the years 2019 and 2020 (Table 2), with 1479 times more chance of occurring compared to the odds of DENV-3 (Table 1). DENV-2 was also the most isolated serotype in 2018 and 2019, according to Lima (2019). In 2020, DENV-2 corresponded to almost half of the cases (49.22%) and in 2019 there was no record of identification of the DENV-3 serotype. According to Furtado (2019), serotype 1 is capable of causing large-scale epidemics in a short period of time, especially in rainy periods, quickly affecting thousands of people. Furthermore, the increase in severe manifestations and severity of disease outbreaks is linked to the concomitant circulation of different types of DENV (FERREIRA, 2018).

Dengue in children can be asymptomatic or manifest itself only as a febrile syndrome. This makes the disease in children under two years of age more difficult to identify, and the first stage of the disease may present with high fever between 39 and 40 degrees, in addition to maculopapular rash on the face, trunk and limbs (MARTINS, 2019). In an Indian study carried out in southern India with the medical records of about 395 children, approximately 99% of the cases in this evaluated population had fever, which was the most common symptom (DASH, 2021).

Although the Ministry of Health (2016)

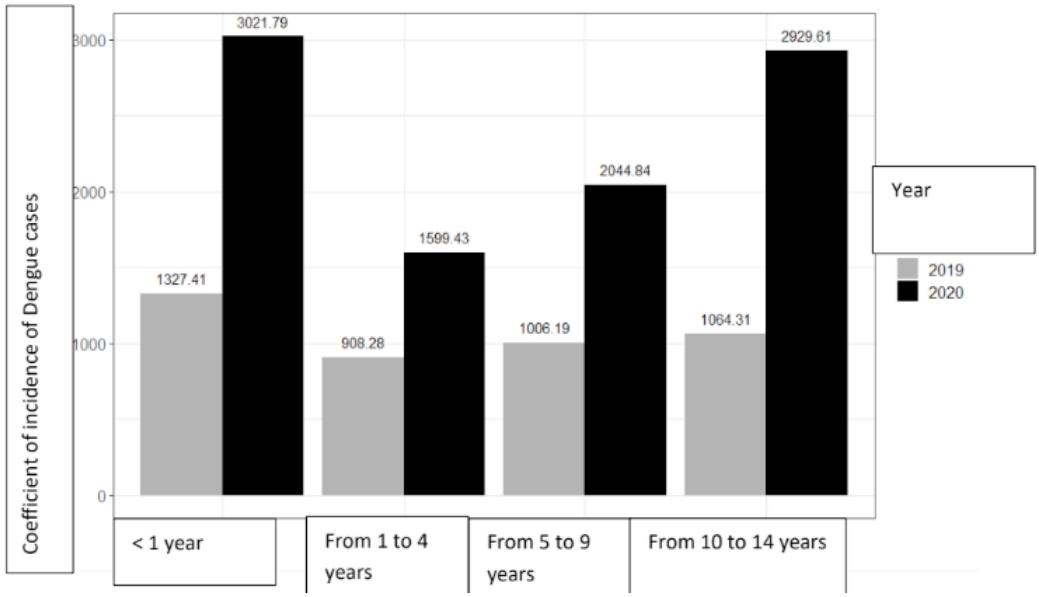


**Figure 1:** Dengue incidence coefficient, by age group (x 100,000 inhabitants). Paraná, 2019 and 2020.

Source: Ministry of Health/SVS/DASNT/CGIAE/SINASC.

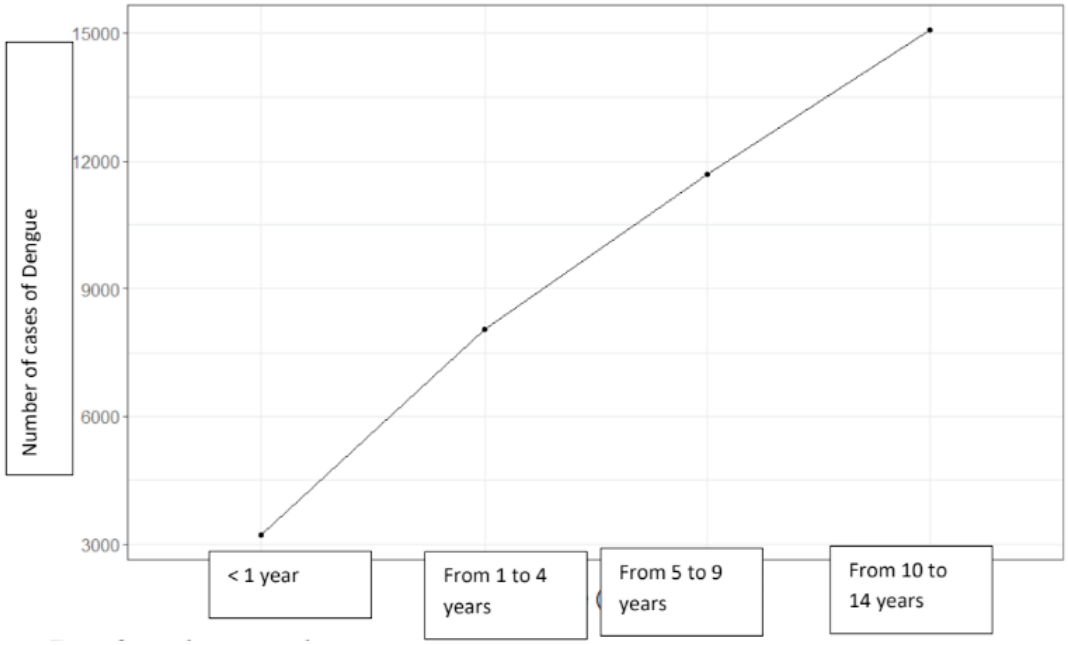


Figure 2: Distribution of the average number of dengue cases notified per year according to age group, in the state of Paraná, in the period 2019 and 2020

Source: Data from the researchers.

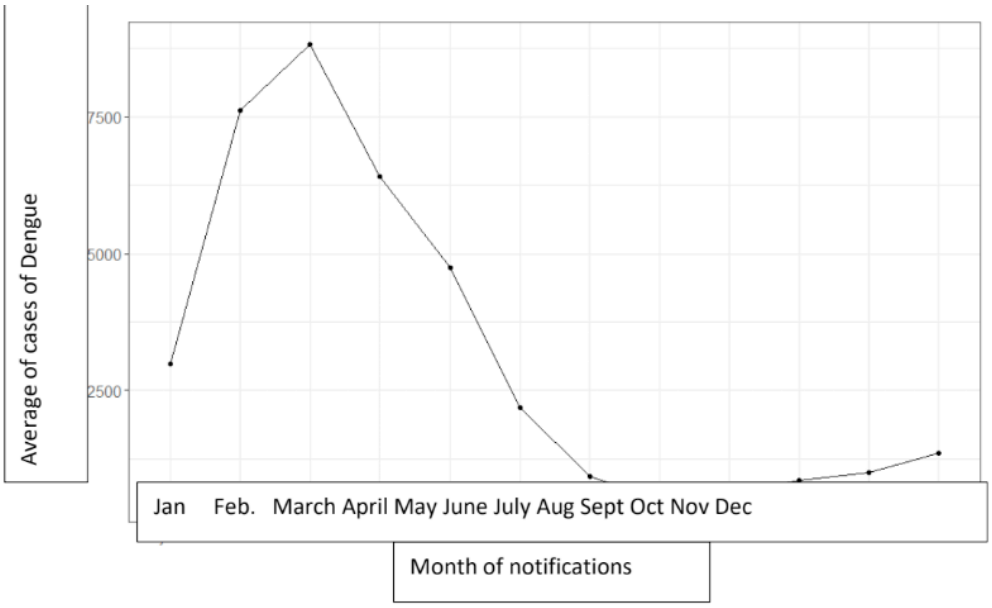


**Figure 3:** Distribution of the monthly average of the number of reported dengue cases in the state of Paraná, in the period 2019 and 2020.

Source: Data from the researchers.

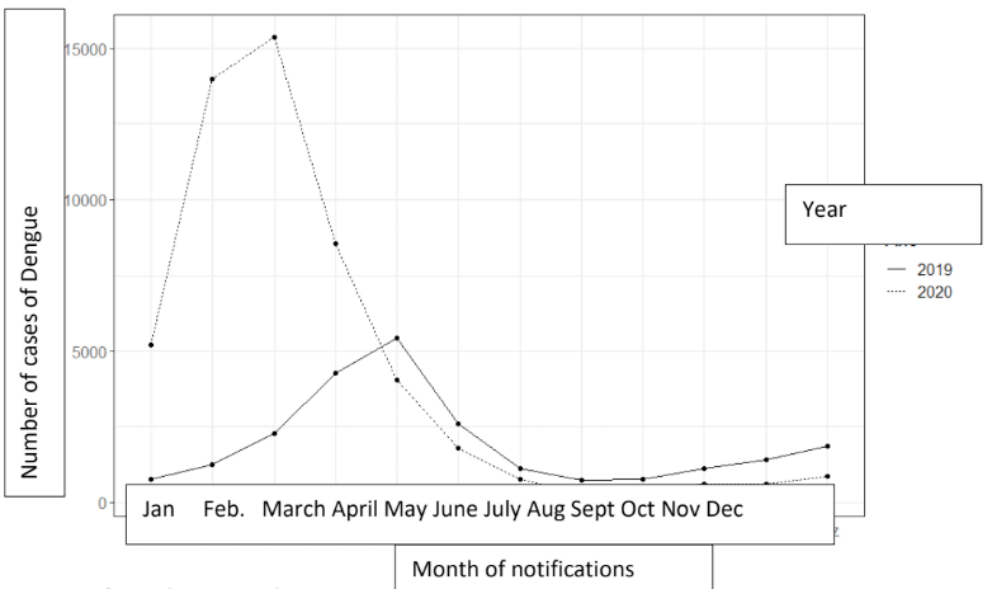


**Figure 4**: Monthly distribution of the number of Dengue cases in children and adolescents aged 0 to 14 years in Paraná, 2019 and 2020.

Source: Data from the researchers.

| Association | Levels | Odds Ratio | Statistic | P-value |
|---|---|---|---|---|
| Age x Dengue Cases | | | 297.01 | 0 |
| | < 1 year | 2.04 | | |
| | 1 to 4 years | 1 | | |
| | 10 to 14 years | 1.82 | | |
| | 5 to 9 years | 1.28 | | |
| Gender x Dengue Cases | | | 1.2 | 0.27 |
| | Female | 1 | | |
| | Male | 1.08 | | |
| Serotype x Dengue Cases | | | 952.92 | 0 |
| | Dengue 1 | 577.59 | | |
| | Dengue 2 | 1479.51 | | |
| | Dengue 3 | 1 | | |
| | Dengue 4 | 48.13 | | |
| Fever x Dengue Cases | | | 221.79 | 0 |
| | < 1 year | 1.99 | | |
| | 1 to 4 years | 1 | | |
| | 10 to 14 years | 1.59 | | |
| | 5 to 9 years | 1.2 | | |
| Year x Dengue Cases | | | 475.82 | 0 |
| | 2019 | 1 | | |
| | 2020 | 4.96 | | |

Table1:Chi-Square Association tests

Source: Data from the Researchers.

| Age | Year | Serotype | Number of cases | % of cases | Incidence |
|---|---|---|---|---|---|
| < 1 year | 2019 | Dengue 1 | 7 | 0.0092% | 4.56 |
| < 1 ano | 2019 | Dengue 4 | 2 | 0.0026% | 1.30 |
| < 1 year | 2019 | Dengue 2 | 18 | 0.0237% | 11.73 |
| < 1 year | 2020 | Dengue 1 | 3 | 0.0039% | 2.05 |
| < 1 year | 2020 | Dengue 2 | 15 | 0.0197% | 10.26 |
| 1 to 4 years | 2019 | Dengue 1 | 29 | 0.0381% | 4.54 |
| 1 to 4 years | 2019 | Dengue 2 | 20 | 0.0263% | 3.13 |
| 1 to 4 years | 2019 | Dengue 4 | 3 | 0.0039% | 0.47 |
| 1 to 4 years | 2020 | Dengue 1 | 12 | 0.0158% | 1.87 |
| 1 to 4 years | 2020 | Dengue 2 | 25 | 0.0329% | 3.89 |
| 1 to 4 years | 2020 | Dengue 3 | 1 | 0.0013% | 0.16 |
| 1 to 4 years | 2020 | Dengue 4 | 1 | 0.0013% | 0.16 |
| 10 to 14 years | 2019 | Dengue 1 | 159 | 0.2091% | 20.92 |
| 10 to 14 years | 2019 | Dengue 2 | 184 | 0.2420% | 24.21 |
| 10 to 14 years | 2019 | Dengue 4 | 21 | 0.0276% | 2.76 |
| 10 to 14 years | 2020 | Dengue 1 | 40 | 0.0526% | 5.32 |
| 10 to 14 years | 2020 | Dengue 2 | 148 | 0.1946% | 19.67 |
| 10 to 14 years | 2020 | Dengue 4 | 1 | 0.0013% | 0.13 |
| 5 to 9 years | 2019 | Dengue 1 | 88 | 0.1157% | 11.59 |
| 5 to 9 years | 2019 | Dengue 2 | 95 | 0.1249% | 12.51 |
| 5 to 9 years | 2019 | Dengue 4 | 18 | 0.0237% | 2.37 |
| 5 to 9 years | 2020 | Dengue 1 | 31 | 0.0408% | 4.03 |
| 5 to 9 years | 2020 | Dengue 2 | 99 | 0.1302% | 12.86 |

**Table 2:** Incidences of serotypes identified in each age group observed individually in the years 2019 and 2020.

Source: Ministry of Health/SVS/DASNT/CGIAE/SINASC.

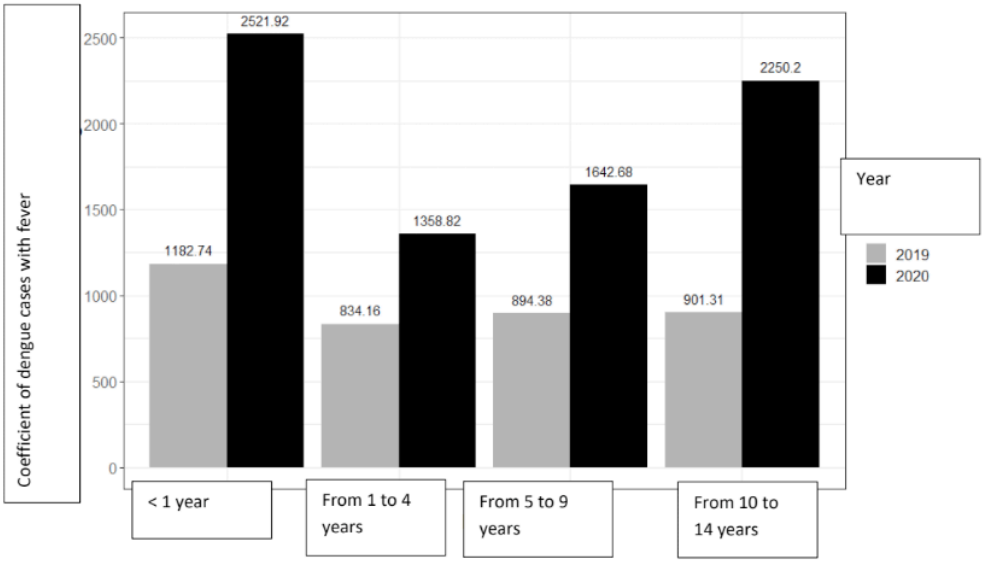


**Figure 5**: Coefficient of incidence of fever in cases of Dengue, by age group (x 100,000 inhabitants). Paraná, 2019 and 2020.

Source: Ministry of Health/SVS/DASNT/CGIAE/SINASC.

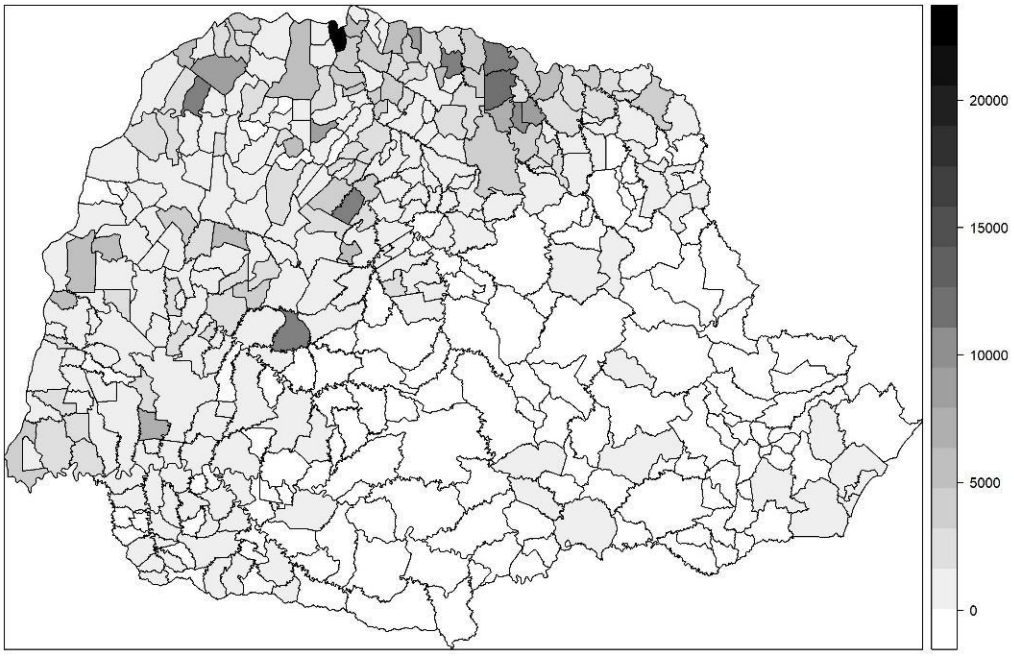


**Figure 6:** Dengue incidence per 100,000 inhabitants in the state of Paraná in 2019.

Source: Ministry of Health/SVS/DASNT/CGIAE/SINASC.

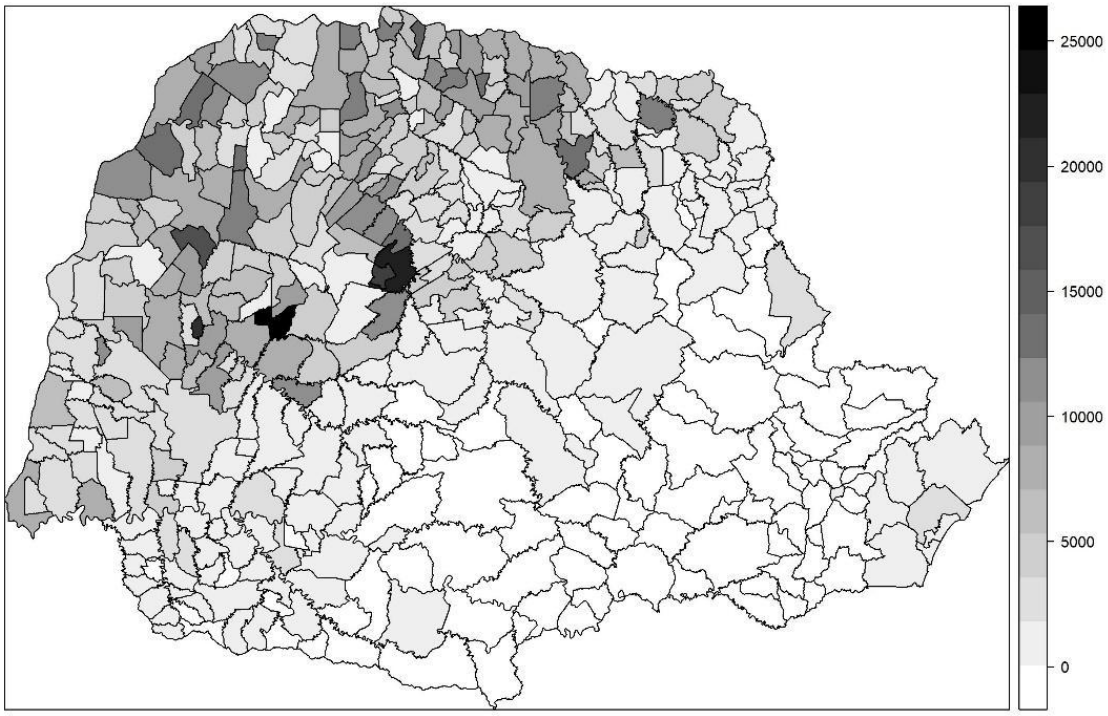


**Figure 7:** Dengue incidence per 100,000 inhabitants in the state of Paraná in 2020.
Source: Ministry of Health/SVS/DASNT/CGIAE/SINASC.

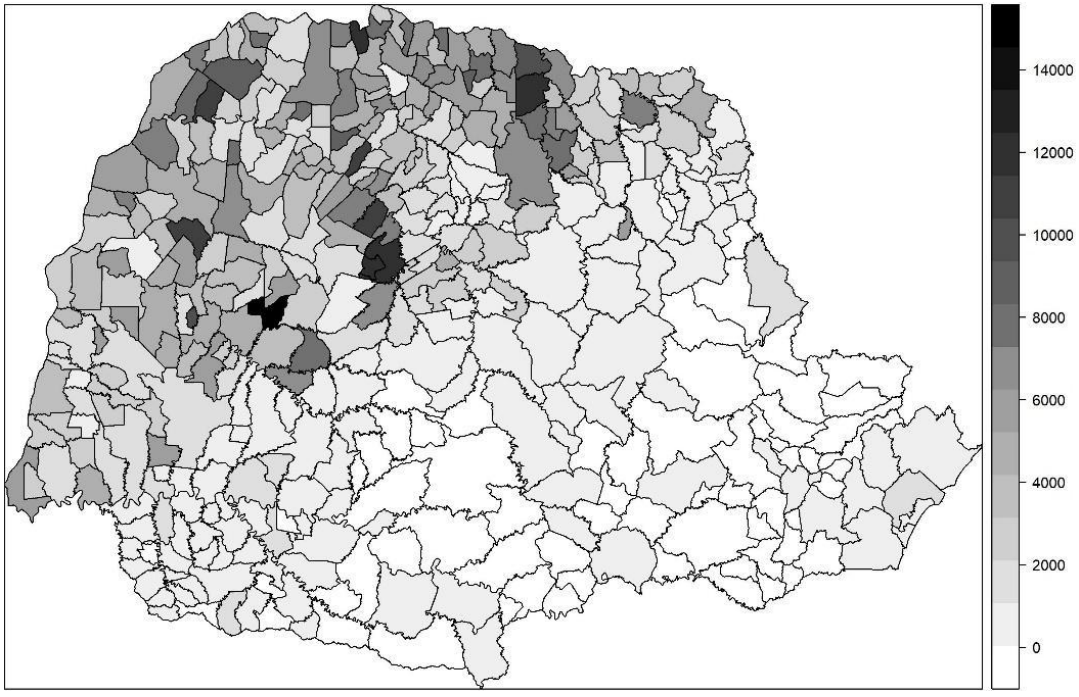


**Figure 8:** Average incidence of Dengue per 100,000 inhabitants in the state of Paraná (2019 and 2020).
Source: Ministry of Health/SVS/DASNT/CGIAE/SINASC.

considers suspected cases of dengue in people with a positive epidemiological history who present: acute fever of less than seven days, associated with two characteristic signs or symptoms of the disease (retro-orbital pain, headache, myalgia, prostration, rash, among others), in the present study, only 15% of the children had fever, which suggests that fever must not be considered a major criterion for suspecting the disease. It was found, with a 95% confidence interval, that children under one year of age are the most affected (= 221.79; p-value < 0.0001) (Figure 5), with 1.98 times more chances of having fever, when compared to to the 1-4-year age group (Table 1).

Other clinical findings considered for suspicion of dengue according to the Ministry of Health (2016), such as the snare test, leukopenia and petechiae, were also significant (Chi-square test, with test statistics = 52025.71, 58701.79 and 39917.16 and p-value < 0.0001 for all cases) (Table 4).

The snare test, although nonspecific, is recommended by the Ministry of Health (BRASIL, 2016). In this study, 8.43% of patients had a positive loop test (Table 4). In an analysis carried out in the municipality of Ubá, in Minas Gerais, medical records of patients with characteristic symptoms of dengue were evaluated. According to the data collected, only 4.68% of adult patients had petechiae (OLIVEIRA, 2020), while in the present study, 13.59% (Table 4).

According to Arruda, in 2019, in the case study of hematological analysis of dengue in children, 68% of the children had leukopenia, while in this study, only 5.85% had a decrease in leukocytes (Table 4). Two possible justifications for this difference: the characteristic of the database used in this work, which deals with secondary data from the notification form sent to the Municipal Health Departments, which are then processed; while in the work by Arruda et al, data are collected directly from the laboratory's database; the other justification would be the possibility of not collecting the blood count in most of these individuals, even with the Ministry of Health's guidance to analyze all children under 2 years of age with suspected disease (BRASIL, 2016).

| Variable | No | Yes | % No | % Yes |
|---|---|---|---|---|
| Prova do Laço | 68926 | 6347 | 91.57% | 8.43% |
| Leucopenia | 70873 | 4400 | 94.15% | 5.85% |
| Petéquia | 65044 | 10229 | 86.41% | 13.59% |

**Table 4**: Percentage of subjects within each snare, leukopenia, and petechiae test category.

Source: Data from the researchers.

The southern region of Brazil had 49,509 confirmed cases in 2019, of which 45,482 were in the State of Paraná (CIRILO, 2020). Changes in demographic and social patterns and the increase in population in recent decades would explain the high incidence of the disease in the region and the difficulties in its control (PESSOA, 2021). It is observed that in Paraná, in 2019, the highest incidence rates belong to the North and Northwest regions of the State, with emphasis on the municipality of Inajá (22,165 cases per 100,000 inhabitants) (Figure 6). In 2020, more municipalities had a high incidence of dengue in children under 15 years of age in Paraná: Juranda (24,675), Barbosa Ferraz (24,597) and Iracema do Oeste (21,971), confirmed cases per 100,000 inhabitants (Figure 7).

When the years 2019 and 2020 are observed together, the North and Northwest regions remain the most affected. In the average incidence of the years 2019 and 2020 (Figure 8), the municipalities that stand out the most are Juranda, Inajá and Sertanópolis (14553, 13205 and 13072 cases per 100 thousand inhabitants, respectively), with a statistically significant difference between the municipalities (= 1090702.05; p-value < 0.0001).

It is known that dengue cases are directly linked to urban conditions such as the amount and method of garbage disposal or any other situations that allow the accumulation of standing water (ALMEIDA, 2020). In Paraná, the most common deposits for mosquito larvae can be removed, such as: bottles, cans, scrap metal, construction debris, tires, potted plants, among others (PARANÁ, 2020). Thus, it is essential to list the importance of the role of the population in this situation, since they can both collaborate for the growth of the disease and help in its control (PESSOA, 2021).

## CONCLUSION

Dengue is an obstacle to public health in most Brazilian regions, causing high morbidity and mortality and public spending. The incidence of this disease in an especially vulnerable group in Paraná is high, with the North and Northwest regions being the most affected. In this sense, it is important to institute measures to contain the disease, since Brazil's own environmental conditions - hot and humid climate, urbanization and precarious basic sanitation in some regions, favor dengue.

This, considered a seasonal disease, had higher rates in April and May 2019 and February and March 2020. During the analyzed period, the most prevalent serotype was DENV-2

It was found that between 2019 and 2020, there was a significant increase in the incidence of dengue cases per 100,000 inhabitants in children and adolescents up to 14 years of age. It was also identified that the most affected age group is children under 1 year old, regardless of gender, which did not show a significant association with the development of the disease. Protective measures for this age group must be encouraged, such as: wearing light-colored clothing with thicker fabrics, with long sleeves and long pants; avoid exposing the child in the first hours before dawn and in the last hours before dusk; put screens on windows and doors; use of mosquito net. Also, considering that most of the children and adolescents affected are of school age, it is essential for schools to participate in the development of campaigns to eliminate the vector, as well as to exemplify the most common symptomatology and warning signs of the disease in children.

As a limitation for carrying out the study, the source of (secondary) information is pointed out, which depends on the adequate process of notification and treatment of these data. To raise this hypothesis, we bring among our findings, a significant discrepancy between the percentage of leukopenia in the individuals of this study and the percentage found in another study with children using the laboratory's own database (Arruda et al, 2019). In addition, there is a possibility of underreporting, justified by the onset of the COVID-19 pandemic in 2020. However, as this is a robust sample, the findings presented here are still valid.

Given the above and the scarcity of studies that address the epidemiology of dengue in children under 15 years of age in Paraná, it is hoped that this will contribute with clinical and epidemiological information focused on this age group, since the incidence of dengue has been increasing considerably in recent years in an especially vulnerable group.

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