

## ORIGINAL ARTICLES

### Mapping Dengue in children in a Colombian Caribbean Region: clinical and epidemiological analysis of more than 3500 cases

#### Running title: Mapping Dengue in Children in a Colombian Caribbean Region

Sandra Milena **Ricardo-Rivera**<sup>1</sup>, Leidy Marcela **Aldana-Carrasco**<sup>1</sup>, Ivan David **Lozada-Martinez**<sup>2,3</sup>, Maria Paz **Bolaño-Romero**<sup>2,3</sup>, Domenica **Acevedo-Lopez**<sup>2,4</sup>, Walter Antonio **Sajona-Leguía**<sup>5</sup>, Daniela Lucía **Bula-García**<sup>6</sup>, Feraz **Fady Zaghhab-Zgieb**<sup>7</sup>, Juan Carlos **Peralta Farak**<sup>8</sup>, Juliana **López Ordóñez**<sup>7</sup>

<sup>1</sup>Department of Epidemiology, Universidad Cooperativa de Colombia, Santa Marta, Colombia;

<sup>2</sup>Medical and Surgical Research Center, Future Surgeons Chapter, Colombian Surgery Association, Bogotá, Colombia;

<sup>3</sup>Grupo Prometheus y Biomedicina Aplicada a las Ciencias Clínicas, School of Medicine, Universidad de Cartagena, Cartagena, Colombia;

<sup>4</sup>School of Medicine, Institución Universitaria Visión de las Américas, Pereira, Colombia;

<sup>5</sup>Grupo de Investigación en Salud Medical Duarte, Clínica Medical Duarte, Cúcuta, Colombia;

<sup>6</sup>Department of Medicine, Universidad del Norte, Barranquilla, Colombia;

<sup>7</sup>Department of Medicine, Universidad de La Sabana, Chía, Colombia;

<sup>8</sup>Department of Medicine, Corporación Universitaria Rafael Nuñez, Cartagena, Colombia

#### *Corresponding author*

Ivan David Lozada-Martinez

E-mail: [ilozadam@unicartagena.edu.co](mailto:ilozadam@unicartagena.edu.co)

## SUMMARY

Dengue continues to be a global public health problem due to its impact in terms of morbidity and mortality and economic burden on health systems, with severe effects mainly on children. Among the objectives of sustainable development is the control of infectious diseases; therefore, it is necessary to evaluate the impact of existing programs on the prevention and management of infectious diseases. The aim of this study was to analyze the epidemiological, clinical, and geospatial behavior of dengue in children in a region of the Colombian Caribbean. A retrospective cross-sectional study was carried out. The data provided by the Municipal Health Secretariat were taken and the cases of dengue and severe dengue in children aged 0 to 17 years reported in Sincelejo, Colombia, were extracted. The sociodemographic and clinical

characteristics presented were analyzed and descriptive statistics were performed with tables and graphs of frequency and accumulated percentages. To locate the areas with the highest incidence of cases during the year, a geospatial location of the cases was carried out with the QGIS v.3.8 program. In 2019, there were 3611 cases of dengue fever in children aged 0 to 17 years. There were 1394 (38.6%) cases with warning signs, and 41 (1.1%) cases of severe dengue fever. Cases of severe dengue fever occurred more frequently in women. The incidence rate found was 3927 and 45.1 cases per 100,000 population, for dengue and severe dengue in children, respectively. The age ranges with the highest number of cases were children aged 4 to 9 years with 1778 cases. The clinical presentation was varied, with the most frequent symptoms, in all groups, being fever in 100% of cases, myalgias  $\geq 71\%$ , and arthralgias  $\geq 64\%$ . Only 9% (n=315) of the cases, corresponded to cases in the rural area. A very high incidence of cases of dengue and dengue with alarm signs in children was evidenced in the Colombian Caribbean region, mainly in the urban area, despite the existence of public health programs and strategies to control the burden of diseases transmitted by arbovirus vectors.

*Keywords:* arboviruses, vector-borne disease, epidemiology, flavivirus.

## **INTRODUCTION**

Diseases transmitted by vectors, bacteria, parasites, and viruses are estimated to be 17% of infectious diseases worldwide, causing 700,000 deaths annually [1-3]. Arboviruses, viruses transmitted by arthropods, mainly mosquitoes, have historically affected human populations through the transmission and circulation of viruses of the Alphavirus and Flavivirus genera, such as Dengue (DENV), Yellow Fever (YFV), West Nile Virus (WNV), and recently Zika (ZIKV) and Chikungunya (CHIKV) viruses [2,4]. Dengue is a vector-borne disease of global public health importance due to its effects in terms of morbidity and mortality and high economic impact on health systems [5]. Dengue disease is caused by one of the four serotypes of DENV, which is endemic in more than 120 countries in the tropics and subtropics. It is estimated that there are more than 50 million viral infections and about 20,000 deaths related to the disease worldwide [1, 2, 6]. In recent years, an increase in the number of cases of DENV has been noted globally, due to the increase in the population growth rate, unplanned urbanization, inadequate water storage, climatic variables, global warming, inefficient mosquito control and globalization [2].

Due to the lack of vaccines, disease control and prevention methods are mostly directed towards the vector, the *Aedes aegypti* mosquito. However, despite the implementation of integrated measures and strategies, the number of cases continues to increase worldwide, with epidemic cycles occurring every three or four years [7-10]. In Colombia, dengue fever is a priority public health problem, since, as in the rest of the world, epidemic peaks occur every three to four years, the last one being the 2019 epidemic which presented a higher number of cases compared to the 2015 epidemic, not only in Colombia but also in the Americas region; Colombia is hyperendemic, and approximately 65% of Colombian municipalities have ecological conditions that favor the sustained circulation of *Aedes aegypti* and the transmission of the dengue virus

(DENV) [3-5, 11]. In addition, the vector is found in all departments of the country, even at previously unrecorded altitudes of 2302 meters above sea level [6].

The city of Sincelejo, for the year 2019 according to the bulletin of the national institute of Colombia, had an epidemiological behavior similar to the rest of the municipalities of the country [12]. Children are an age group very frequently affected by this condition, so most of the strategies are aimed at protecting this population group [1,3,10]. Considering objectives of global health, priorities of global public health and the continuous evaluation of the performance of vector-borne disease prevention programs, the aim of this study was to analyze the clinical, epidemiological and geospatial behavior of dengue fever in children in a major Colombian Caribbean city during 2019, and discuss the results according to the health priorities of the region.

## **MATERIALS AND METHODS**

### *Study design*

Retrospective cross-sectional study, which included children aged 0 to 17 years with a diagnosis of dengue fever, in the city of Sincelejo, Colombia, during the year 2019. The city of Sincelejo is located in northeastern Colombia (9°17'58"N 75°23'45"W), with an area of 284.4 km<sup>2</sup> and a population for 2019 of 286,635 inhabitants, of which 43,258 were boys and 47,568 were girls. The pediatric population data from the municipal health department were used. The urban area of Sincelejo is organized into 9 communes and 224 neighborhoods.

### *Variables assessed and data extraction*

The information was extracted from the dengue and severe dengue notification bulletins of the municipality, serving as the unit of analysis. The database was organized and filtered, and the sociodemographic and clinical variables were selected. The variables evaluated were: clinical manifestations, age, sex, area of origin, severity of the case, paraclinical alterations, and associated complications.

### *Data analysis*

For data analysis, the data were organized in the Excel program and divided into cases according to their final classification, dengue without alarm signs, dengue with alarm signs, and severe dengue. The data were analyzed using descriptive statistics with tables and graphs of frequency and percentages. Likewise, the incidence rate of dengue in children was calculated according to its classification per 100,000 population. To calculate the dengue incidence rate, the numerator used was the total number of dengue cases minus the number of severe dengue cases. Dengue incidence rate and severe dengue incidence rate were calculated separately. The denominator was represented by the total number of children living in the city (n=90,826). To locate the neighborhoods with the highest incidence of cases during the year, a geospatial location of the same was carried out with the QGIS v.3.8 program.

### *Ethical statements*

This study was exempt from approval by the ethics committee, because the information extracted and analyzed is published by the city's governmental health entities. However, it complied with

the Declaration of Helsinki, and was classified in the category of research without risk, according to article 11 of Resolution 8430 of 1993 of the Colombian Ministry of Health [13, 14]. All patients or their relatives signed the informed consent form. The management of the data obtained from the medical records was carried out in accordance with the provisions of Law 23 of 1981 of the Colombian Congress and Resolution 1995 of 1999 of the Colombian Ministry of Health [15, 16].

## RESULTS

A total of 3611 cases of dengue fever was obtained for 2019 in children aged 0 to 17 years in the city of Sincelejo. There were 2173 (60.2%) cases of dengue without alarm signs, 1,394 (38.6%) cases with alarm signs, 41 (1.1%) cases of severe dengue and three unclassified cases (0.1%) (Table 1). The age range with the highest number of cases was 4 to 9 years with 1,778 cases, followed by the age range 10 to 12 years with 650 cases. The age range with the lowest number of cases was 16 to 17 years with 171 cases. The distribution of cases according to sex had an equal proportion (males; n=1820 vs. females; n=1788). However, there were more cases of severe dengue fever in females with 26 cases compared to 15 cases in males. The incidence rates found were 3927 and 45.1 cases per 100,000 population, for dengue and severe dengue in children, respectively.

About the presentation of cases by month, there was an increase in May to June from the notification of 112 cases to 218, with a maximum peak in September with 571 cases reported and then a decrease in the following months, finally with the report of 240 cases for December (Figure 1). In the second period of 2019, 74.1% of the notifications of dengue cases were presented.

For children who were classified as dengue without alarm signs, the most frequent symptoms were fever, myalgias, arthralgias, headache, and to a lesser extent, skin rash and retro-ocular pain (Table 2). For those classified as having dengue with alarm signs, the majority presented fever, myalgias, headache, intense and continuous abdominal pain, arthralgias, and persistent vomiting. To a lesser extent, they presented drop in platelets, diarrhea, somnolence, hemorrhages, increased hematocrit, fluid accumulation, hypotension, and hepatomegaly (Table 2). Finally, those classified as severe dengue presented symptoms such as fever, drop in platelets, myalgias, intense and continuous abdominal pain, arthralgias, persistent vomiting, headache, and severe organ damage. To a lesser extent, hemorrhage with hemodynamic compromise, significant mucosal bleeding, and hypothermia (Table 2).

In the identification of the neighborhoods by communes in Sincelejo, it was evident that all the communes of the city presented at least one neighborhood with a report of more than 30 cases. The commune that presented the highest number was commune 8 with seven neighborhoods, followed by commune 6 with six neighborhoods, commune 1 with five neighborhoods, commune 2 with four neighborhoods, commune 7 with three neighborhoods, communes 3 and 9 with two neighborhoods each, and finally communes 4 and 5 with one neighborhood each (Figure 2).

Likewise, it was possible to identify the neighborhoods that during 2019 reported a high incidence of dengue fever, with a notification of more than 56 cases eight neighborhoods were identified, those were for commune 1 the Villa Paz neighborhood, Camilo Torres for commune 2, Pioneros in commune 3, Las Mercedes in commune 4, Botero in commune 6, and the neighborhoods Villa Mady, El Poblado and Puerto Arturo in commune 8.

Comento [sn1]: ???

Of the 3611 cases reported, 9% (n=315) corresponded to cases of dengue fever in children reported in townships and rural areas of the city of Sincelejo. The cases occurred mainly in the townships of Chochó, La Gallera, La Arena, Las Palmas, San Antonio, Cerrito la Palma, among others; however, cases were reported in rural areas of Sincelejo from Buenos Aires, Cerrito Colorado, La Garita and Villa Rosita.

## DISCUSSION

Colombia is one of the countries in the Americas most affected by dengue, especially in 2019, as could be seen in the study by Zambrano et al. where Colombia was the second most affected country, also directly affecting the population under study in our work [4]. Carrying out a comparison of the results presented by Salgado et al., it is valid to emphasize that the number of cases of severe dengue was significantly higher in the work carried out in 2017 as opposed to our research in the city of Sincelejo [17]. Similarly, the same percentage pattern is still evident in the study conducted by Torres et al., within the criteria for the classification of dengue in children, but there is a minimal increase in cases of severe dengue, compared to that obtained in the present study [18].

Although the infection figures were much higher in other studies compared to the current one developed in the city of Sincelejo, this may be due to macro and micro determinants in the study populations, such as social, environmental, life factors, or physiological factors, as well as population densities in the sampling sites. On the other hand, by finding variations in various studies concerning dengue cases and sex, it can be established that there was no prevalence of one sex over the other. Dengue infection in children is very heterogeneous, which is demonstrated in the current study and contrasted with others, and it is shown that both genders have the same risk of suffering the disease.

Regarding the behavior concerning age, the results of our study were similar to the study conducted by Chaves et al, who reported that the predominant age groups were patients aged 0 to 9 years, followed by 13.4% corresponding to patients aged 10 years or more which in many occasions is unusual [19]. However, they also argue that as in this case, the incidence in children of this age group may be due to factors that influence the circulation dynamics of *Aedes aegypti*, i.e., as the mosquito is a diurnal species, with greater activity in mid-morning and shortly before dark, it may pose a risk to children who are at school or playing outside [19].

The increase in dengue cases is associated with the increase in rainfall and changes in the climatic season that corresponds to the "La Niña" phenomenon, between the months of June and December. Thus, in the present study, we can notice a significant increase in dengue cases in the

pediatric population starting in June, with the highest peak in September with 571 cases. For the second period of 2019, a total of 2677 cases of dengue fever in children were reported for the city of Sincelejo, that is an extremely high proportion with respect to what was reported in the first semester (n=890), similar to the obtained by Fernández Hernandez & Ledesma Paniza, where it was determined that the high incidence of dengue cases in different areas of the departments of Colombia may be due to climatic changes with the increase in temperature and population growth often poorly planned, which has allowed the establishment of mosquitoes and transmission of the disease in unusual places [20]. Based on the above, we can corroborate the importance of the statement by Zambrano et al. on epidemiological mapping as a tool of great impact for countries and regions with epidemics of vector-borne diseases, which need to be constantly monitored over time, to see the effectiveness of public health programs [21].

Commento [sn2]: that?

A more detailed analysis shows that in the three stages of dengue classification, fever tends to be a common denominator in these cases, presented in 100% of dengue patients with or without warning signs and cases of severe dengue. Other symptoms that occur in high percentages in pediatric patients in the different stages of dengue are headache, myalgia, and arthralgia [22, 23]. The variations lie in the symptoms of dengue with alarm signs where high percentages of patients with severe abdominal pain and vomiting appear. In addition to what has already been mentioned, in cases of severe dengue, there is also a significant number of infants with decreased platelets and serious organ damage [24, 25]. Those results obtained in the research can be supported by other studies that demonstrate the same behaviors in terms of symptom presentation [22-25].

Commune 7 was the sector with the highest number of neighborhoods with dengue cases in the city of Sincelejo. The neighborhoods included in this commune are characterized by being informal or squatter neighborhoods, in the entire periphery surrounding the Troncal de Occidente highway. These households have socioeconomic characteristics that, in more detail, end up being macro and micro determinants of transmission. Most of the population do not have or have not completed school education levels. They also have major deficiencies in basic sanitation, lack public services and have a high population density, and all these factors play an important role in the spread of the vector and the dengue virus.

It is known that some rural areas do not have solid waste collection services and aqueducts and sewage systems. The negligence leads the rural population to collect and accumulate water in containers (jars and tanks). Now, due to the lack of knowledge that the people have about dengue, they tend to store water inadequately, creating habitats where the vector that transmits the disease reproduces. Similarly, containers located inside homes in dark, uncovered spaces provide attractive breeding sites for the vector. Another factor inducing the presence of dengue is the density of homes, *i.e.*, the greater the number of houses, the greater the probability of infection by the dengue virus. This behavior was evidenced in the results, where the townships with a higher population index had more cases of infected children compared to those in rural areas that tend to be much more dispersed.

Thus, it can be observed that there are still failures in the implementation and fulfillment of strategies established by international consensus and scientific societies for the control of this

type of diseases, which are a priority for public health in the region. Once again, health education and the help of the community is an indispensable determinant for the control of vector-borne diseases. The risk factors described above can be controlled by these actors, especially in rainy seasons that favor the biological cycle of the Aedes vector [26, 27]. It is necessary to reinforce public policies, invest in a greater number of programs, which are more intense in regions with a critical trend of more severe cases, which also present difficulties in accessing specialized medical services, in order to substantially reduce morbidity and mortality. In order to accurately define the impact of these strategies, it is imperative to conduct ongoing epidemiological and eco-epidemiological studies to identify strengths and weaknesses. As a limitation of this study, it is necessary to consider the bias of analysis and interpretation, because our analysis depends on the available data, which are not personally verifiable.

## CONCLUSION

A very high incidence of cases of dengue and dengue with alarm signs in children was evidenced in the Colombian Caribbean region, mainly in the urban area, despite the existence of public health programs and strategies to control the burden of diseases transmitted by vectors. It is necessary to reevaluate the possible causes of this behavior and reinforce health strategies and public policies to achieve the goals established by global consensus and contribute to the reduction of the disease burden of vector-borne diseases.

## DECLARATION OF CONFLICTING INTEREST

The authors declare that there is no conflict of interest.

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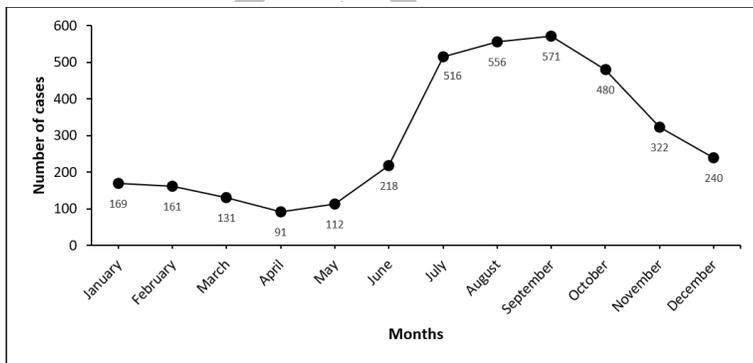
**Table 1 -** Classification of the total number of dengue cases observed in the pediatric population evaluated.

Classification	No. cases
Dengue without warning signs	2173
Dengue with warning signs	1394
Severe dengue	41
Unclassified	3

**Table 2 -** Presentation of signs and symptoms of dengue without alarm signs, with alarm signs and severe dengue in pediatric population in Sincelejo during 2019.

	Total frequency of signs and symptoms presented	Cumulative percentage
<b>Dengue without warning signs</b>		
	(n)	
Fever	2173	100%
Myalgias	1727	79%
Arthralgias	1383	64%
Headache	1380	64%
Rash	782	36%
Retroocular pain	630	29%
<b>Dengue with warning signs</b>		
Fever	1394	100%
Myalgia	1113	80%
Headache	1037	74%
Intense and continuous abdominal pain	899	64%
Arthralgias	873	73%
Persistent vomiting	696	50%
Retroocular pain	526	38%
Rash or rash	495	36%
Drop in platelets	433	31%
Diarrhea	271	18%
Drowsiness or irritability	71	5%
Significant mucosal bleeding	67	5%
Increased hematocrit	60	4%
Fluid accumulation	28	2%

Hypotension	19	1%
Hepatomegaly	17	1%
<b>Severe engue</b>		
Fever	41	100%
Drop in platelets	32	78%
Myalgia	29	71%
Severe and continuous abdominal pain	29	71%
Arthralgias	28	68%
Persistent vomiting	28	68%
Headache	26	63%
Severe organ damage	24	59%
Retroocular pain	18	44%
Fluid accumulation	17	41%
Increased hematocrit	16	39%
Severe plasma extravasation	16	39%
Rash or rash	15	37%
Drowsiness or irritability	11	27%
Dengue shock	10	24%
Hypotension	8	20%
Diarrhea	7	17%
Hepatomegaly	7	17%
Hemorrhage with hemodynamic compromise	6	15%
Significant mucosal bleeding	4	10%
Hypothermia	2	5%



**Figure 1** - Number of dengue cases in pediatric population per month reported in Sincelejo in 2019.

**Figure 2** - Neighborhoods with reported more than 30 cases of dengue fever in children aged 0-17 years in Sincelejo, 2019.

