

A finding that could change what we know about dengue in Colombia

Dengue is an old global public health threat that lashes out stubbornly through cycles in tropical countries. It gives truce for a few years and then comes back stronger in specific seasons. 2023, for example, is one of those periods when this mosquito-borne disease has been unleashed in Colombia.

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According to public data from the Instituto Nacional de Salud (INS) (National Institute of Health), every day this year, on average, 312 cases of dengue have been registered, a figure that represents almost double what was seen in 2022 and that will surely be located in the historical records for an outbreak that has had the vast majority of territorial entities on alert.

In such a complex and emergency scenario, a group of researchers of Universidad del Rosario has followed up on a finding that could change what we know about dengue in the country and that, without further ado, demands that we pay greater attention to the behavior of this disease.

This is no less than the introduction and possible circulation of the Cosmopolitan genotype of dengue in Colombia, a variant that has been responsible for strong outbreaks in oth-

er latitudes and is still being studied if it has more severe clinical manifestations.

The *Aedes aegypti* mosquito inhabits almost the entire national geography, from the departments bathed by the Atlantic and Pacific oceans, through the immensity of the Eastern Plains, to deep in the lush jungles of the south. It could well be said that the tropical and humid characteristics of our country are ideal for this insect to reproduce and spread diseases such as dengue, Zika and chikungunya.

And while the fight against this vector of transmission adds decades of efforts, in recent years there have been recurrent outbreaks in three-year cycles, the most notable being those recorded in 2016 and 2019, when 80 111 and 74 898 cases were counted respectively. In 2023, according to INS data cut as of September 16, the number of patients exceeded those records: 80 461; 44.1 percent of them had warning signs and 1.4





Rosario researchers analyzed 120 dengue-positive samples.

percent had the most severe form of the disease.

[Giovanni Rubiano](#), director of the National Institute of Health (INS), states that the alarming statistics this year can be explained by the cyclical behavior of this epidemic and also because “the intense climatic variability of recent periods, the El Niño phenomenon and other conditions typical of tropical climates such as ours make the proliferation of the transmitting mosquito more likely.”

In addition to these factors, there is a line of research that tries to establish if there have been changes in the dynamics of this [endemic](#) in the country following the arrival of a new variant of the virus, the Cosmopolitan, which was already detected in two departments and, as suggested by early studies, could potentially increase the severity of the disease or intensify its circulation in the territory.

Under this hypothesis the research developed in recent years has been led by [Juan David Ramírez González](#), PhD, associate professor at Universidad del Rosario and scientific director of the Centro de Investigaciones en Microbiología y Biotecnología in this institution ([Cimbiur](#)) (Center for Research in Microbiology and Biotechnology).

Ramírez and his team try to decipher dengue in Colombia by focusing on genomic surveillance of the virus, that is, by investigating, through laboratory tests, the origin of circulating serotypes and their possible genetic variations in mosquito and patient samples.

In September 2022, for example, they published in the scientific journal [Frontiers in Ecology and Evolution](#) a study in which they



analyzed mosquito vectors in several departments of the country and found, in addition to some cases of coinfection (insects carrying two or three serotypes of the virus at once), that there is already a transition in the prevalence of dengue serotypes circulating in Colombia, which goes from serotype 1 to serotype 2 as the most predominant in the mosquito population.

Ramírez explains that “dengue has four serotypes; the most dominant in our country are 1 and 2. The latter is frequently associated with more severe infections and epidemics. During 10 years of surveillance serotype 1 was responsible for 60 percent of cases and 2 for 40 percent, but we are currently observing the opposite and the dominance is serotype 2 in that same proportion. We do not know the reasons why this is happening because because



“We need a clear pathway for dengue prevention from vector control and monitoring, case surveillance, and genomic evaluation. However, it is also very important to raise awareness about the mechanisms of transmission and that people understand that it is a disease that can be prevented,” emphasizes researcher Juan David Ramírez .

of the pandemic we had three years in which there was no further information.”

Ramírez points out that this change could be explained by climatic, ecological or epidemiological variables. However, one of the potential hypotheses they explore is precisely whether the introduction of new variants – as in Covid-19 – of serotype 2 made it more transmissible and with greater development in the vector.

These variants are actually genotypes, and dengue serotype 2 has at least five, the INS technical release details. One of them, the variant named the Cosmopolitan, is now being targeted as the potential responsible for this transition.

The Cosmopolitan in Colombia

On 4 July, 2023 the INS [sent a technical statement](#) to the territorial entities through which it reported the identification of the

circulation of the Cosmopolitan dengue genotype in Colombia. Specifically, PCR analysis conducted between March and April found this genotype present in 11 samples collected in the Amazon. In that document, the INS acknowledges that between 2021 and 2022, the only identified dengue serotype 2 genotype in the country was one known as the Asian-American genotype.

According to the Institute, virological surveillance regarding this variant was activated by the history of Peru, Brazil and Ecuador, where, according to scientific research, the Cosmopolitan was responsible for the increase in dengue cases.

This variant is already circulating in different regions of the world, mainly in Asia, and the first case in South America was identified in 2019 in Peru. Subsequently, one case was reported in Brazil in November 2021. In all locations where it has been identified, it has caused specific increases in virus circulation.

And while the INS in the same July document said that the Cosmopolitan variant was not found in samples sent by 19 other depart-

ments between November 2022 and May 2023, the team led by Ramírez did manage to confirm it recently in patients from Meta, suggesting that this version of the virus has already spread to at least one other Colombian region apart from the Amazon.

Specifically, the researchers of Universidad del Rosario analyzed 120 dengue-positive samples collected between April and May in Meta and performed complete sequence of the virus genome. Most were of the Asian-American genotype, but two were of the Cosmopolitan variant, according to the study that was accepted for publication in the journal *Emerging Infectious Diseases*.

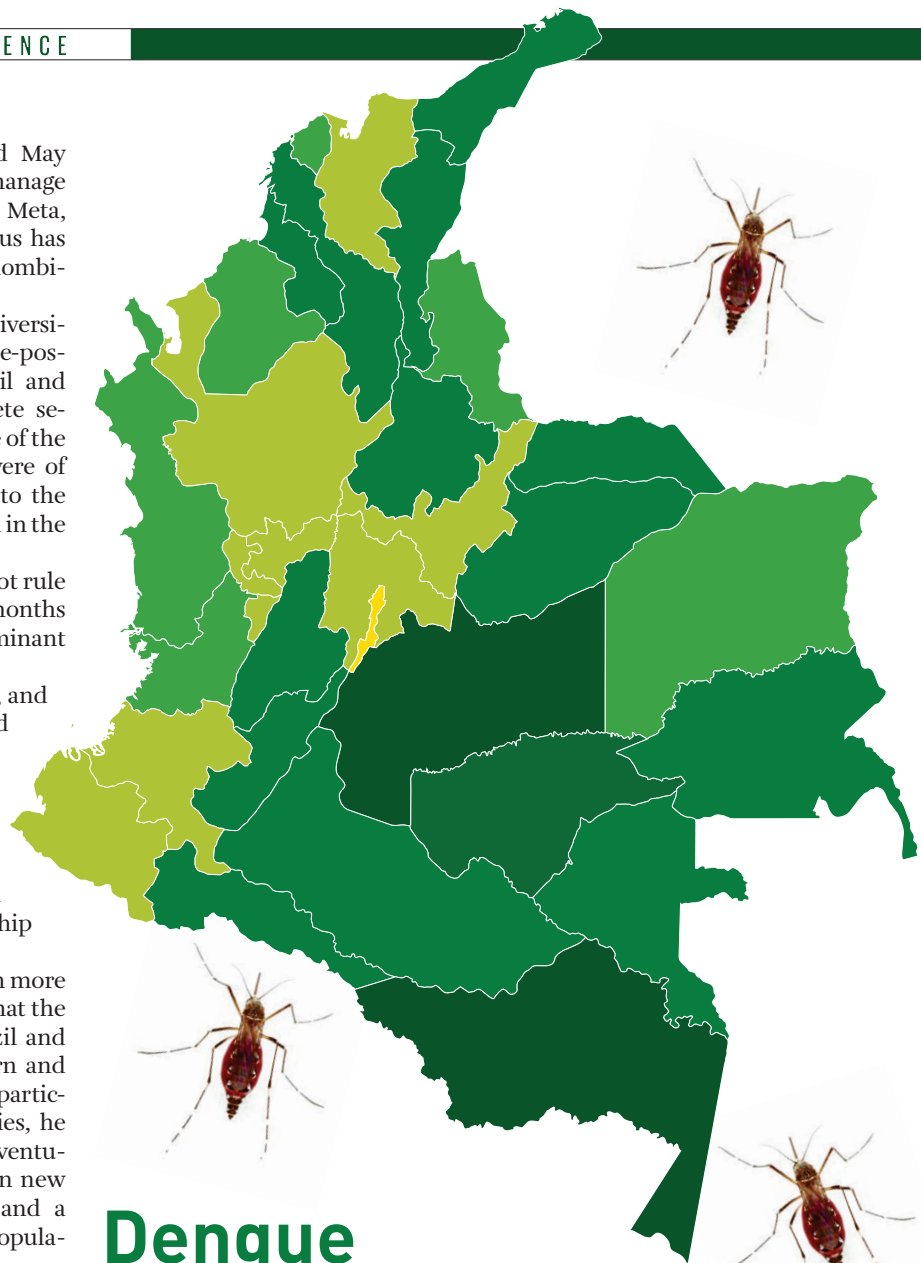
Ramírez prefers caution, but does not rule out a scenario where in the coming months the Cosmopolitan variant becomes dominant in the country.

[Félix Delgado](#), PhD in immunology, and associate researcher of Universidad El Bosque, confirms that “as seen in countries like Peru, there is an initial epidemiological association between the presence of this the Cosmopolitan variant and the increase in cases of severe dengue and even Guillain-Barré, although this relationship needs further investigation.”

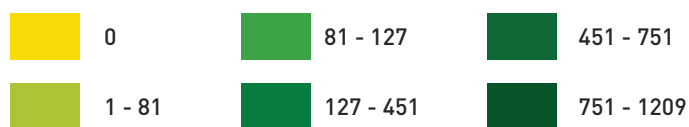
Rubiano, on the other hand, is much more cautious and although he recognizes that the natural history of this variant in Brazil and Peru showed a more infectious pattern and that it can produce serious disease, in particular, in older adults with comorbidities, he points out that it is not known if an eventual expansion in Colombia “could mean new premature outbreaks in the future and a significant affectation to vulnerable populations.”

“It can happen that, due to the biological conditions of humans and vectors, as well as small changes of the virus, it loses part of its characteristics. Evidence available in other countries suggests that it is too early to infer any significant change in Colombia. To date, the cases that have been confirmed infected with this genotype have had mild forms of the disease and therefore it is necessary to reiterate that it is not appropriate to define the impact of the virus in the country until more evidence is achieved elsewhere and its possible distribution and dispersion in Colombia is not known more thoroughly,” states Rubiano.

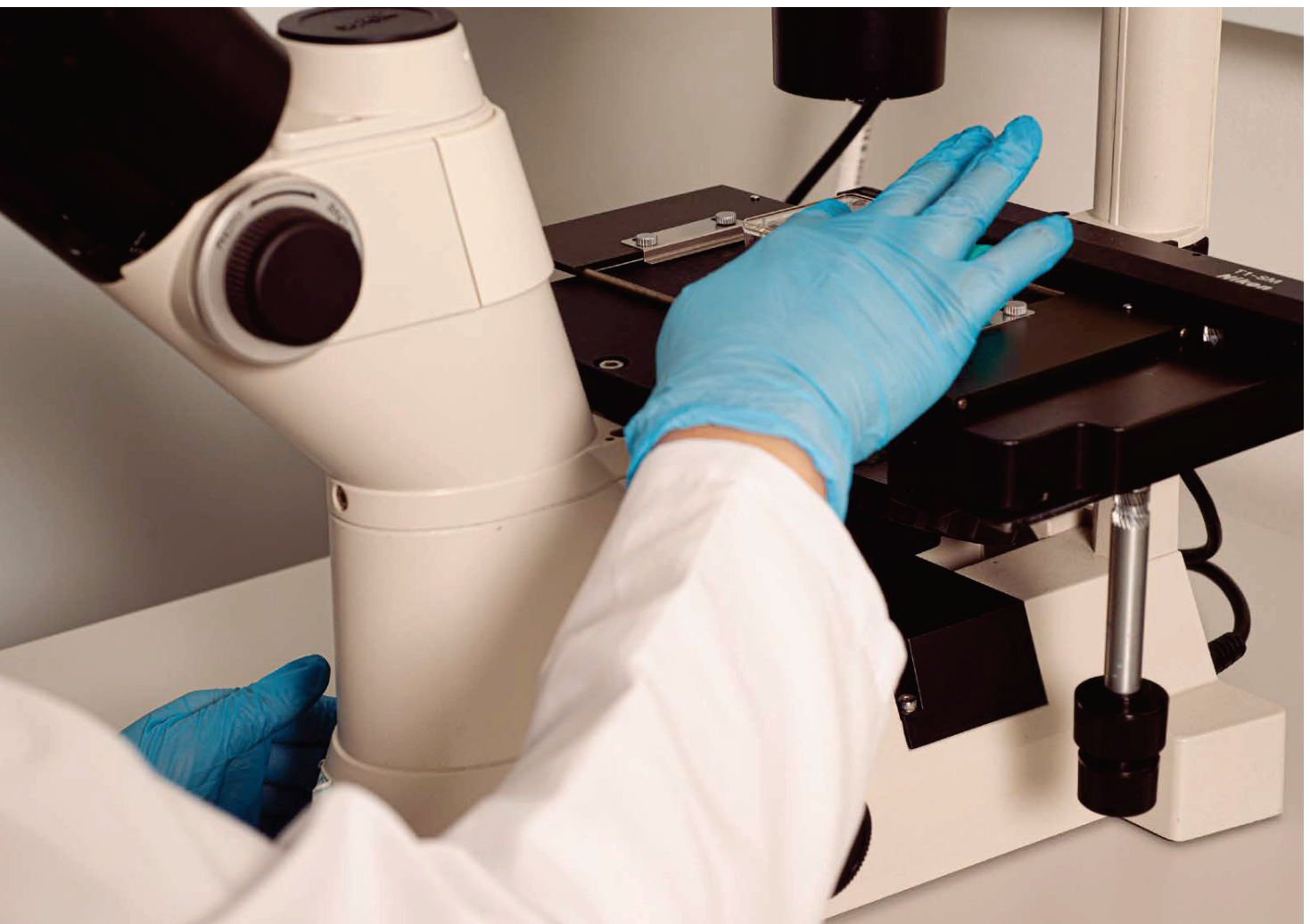
For [John Mario Gonzalez](#), PhD in Immunology and professor of Universidad de los Andes, there is an important point of consideration regarding the arrival of the Cosmopolitan variant in the country and it is the factor of antibodies. “When a person gets



Dengue incidence in 2023 per 100 000 Inhabitants



Source: National Institute of Health, October 2023.



sick with dengue, regardless of the serotype it is, they develop immunity against it. Severe forms occur when we are infected by a serotype for which we have no defenses. And since the Cosmopolitan is a new variant, the immune response may be different,” she explains.

Eyes open

Dr. Ramírez points out that for the time being it is urgent to establish whether there may be a dominance of this variant in Colombia and therefore together with his team they continue to sequence virus from patients from months after May and in other departments. “We want to know if it has spread, because in less than a month it went from the Amazon to the Meta. It is very likely that in other departments of the country it is also present, but we must determine it and, from there, try to understand how these mutations can be involved in more infectivity, in more transmissibility or in more aggressiveness,” says the researcher.

Rubiano agrees on this need to continue virological surveillance and reports that “during 2022 and 2023, the largest number of dengue genome sequences have been obtained, taking into account the surveillance needs associated with outbreaks in the country and international alerts on circulation of new viral genotypes such as the Cosmopolitan.”

For this purpose, there is the permanent availability of 33 public health laboratories throughout the national territory, as well as the National Reference Laboratory (affiliated to the INS) of the country, where samples of cases with severe dengue or deaths from this cause are processed.

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“This capacity can be expanded, as was done at the time for Covid-19, with the participation of service delivery institutions, research institutions or universities that, taking advantage of their installed capacity, could support genomic surveillance,” concludes the director of the INS.

While these investigations are progressing, the researcher Ramírez calls for prioritizing dengue as a public health problem and emphasizing its prevention and control in a comprehensive way. “We need a clear pathway for dengue prevention from vector control and monitoring, case surveillance, and genomic evaluation. However, it is also very important to raise awareness about the mechanisms of transmission and for people to understand that it is a disease that can be prevented,” emphasizes the professor of Universidad del Rosario.

As important as investigating the origins of circulating variants, Ramírez notes, is to educate people about the mechanisms of transmission and to raise awareness that dengue is a disease that can be prevented with self-care measures, such as proper vector and hatchery control, insect identification, the use of repellents, and more education on the subject in general. ■