Hidden 'super spreaders' spur dengue fever transmission, finds study

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A NASA satellite image shows the metropolitan area of Iquitos, Peru, nestled in the Amazon Basin, on the banks of the Amazon River and surrounded by smaller rivers, lakes and lagoons. Credit: NASA

For mosquito-borne diseases such as dengue fever, the abundance of the insects in places where people gather has long served as the main

barometer for infection risk. A new study, however, suggests that the number of "hidden" infections tied to a place, or cases of infected people who show no symptoms, is the key indicator for dengue risk.

PNAS Nexus published the research led by scientists at Emory University, which drew from six years of data collected in the Amazonian city of Iquitos, Peru.

The results found that 8% of human activity spaces in the study accounted for more than half of infections during a dengue outbreak. And these "super spreader" spaces were associated with a predominance of asymptomatic cases, or 74% of all infections.

"Our findings show that any public health intervention that focuses on responding to symptomatic cases of dengue is going to fail to control an outbreak," says Gonzalo Vazquez-Prokopec, first author of the study and an Emory associate professor of environmental sciences. "Symptomatic cases represent only the tip of the iceberg."

Co-authors of the research include Uriel Kitron, Emory professor of environmental sciences; Lance Waller, professor of biostatistics and bioinformatics at Emory's Rollins School of Public Health; and scientists from University of California-Davis, Tulane University, San Diego State University, University of Notre Dame, North Carolina State University and the U.S. Naval Medical Research Unit in Lima, Peru.

'What matters is where you went'

Dengue fever is caused by a virus transmitted by the bite of a female Aedes aegypti mosquito. When the insect takes a blood meal from a human infected with dengue, the virus begins replicating within the mosquito. The virus may then spread to another person that the mosquito bites days later.

This species of mosquito feeds exclusively on human blood, has a limited flight range of about 100 meters and thrives in sprawling urban areas of the tropics and subtropics. Its preferred habitat is inside homes, where it rests on the backs of furniture and at the bases of walls. Even the little bit of water held by an upturned bottle cap can serve as a nursery for its larvae.

Vazquez-Prokopec is pioneering new mosquito-borne disease interventions, including tapping spatiotemporal data to track, predict and control outbreaks of pathogens transmitted by Aedes aegypti. The mosquito spreads the Zika, chikungunya and yellow fever viruses in addition to dengue.

Around 500,000 cases of dengue occur annually around the world, according to the World Health Organization. The disease is caused by four distinct but closely related serotypes of the dengue virus. Infected people may have some immunity that prevents them from experiencing any noticeable effects while others may be severely debilitated for a week or more by symptoms such as extreme aches and pains, vomiting and rashes. Dengue hemorrhagic fever, the most severe form of the disease, causes an estimated 25,000 deaths annually worldwide.

Iquitos, a city of nearly 500,000 people on the edge of the Amazon rainforest in Peru, is a dengue hotspot. For more than a decade, Vazquez-Prokopec and colleagues have mapped patterns of human mobility and dengue spread in Iquitos.

"For diseases that are directly spread from one person to another, like COVID-19, what matters is who you were near," he says. "But in the case of dengue, what matters most is where you went."

Tracking hidden cases

For the current study, the researchers wanted to determine the role of asymptomatic cases. People without symptoms may continue to go about their daily routines, unknowingly infecting any mosquitoes that bite them, which can then later spread the virus to more people.

The study involved 4,600 people in two different neighborhoods. They were surveyed three times a week about their mobility. This data was used to map "activity spaces," such as residences, churches and schools.

The study participants were also regularly surveilled to determine if they experienced any dengue symptoms. Blood analyses confirmed a total of 257 symptomatic cases of dengue during the six-year study period. That led to investigations of other participants whose activity spaces overlapped with the symptomatic cases. More than 2,000 of these location-based contacts were confirmed by blood tests to have dengue infections and more than half of them reported not having any noticeable symptoms.

A cascade of circumstances

The results pinpointed the role of asymptomatic "super spreaders" in a dengue outbreak. A small number of the activity spaces, or 8%, were linked to more than half of the infections and most of the cases associated with those places were asymptomatic.

The comprehensive, one-of-a-kind study broke down the virus infections by serotype and measured the amount of mosquitoes in the activity spaces.

"We found that the mosquito numbers in a location alone is not a predictor of the risk of infection," Vazquez-Prokopec says.

Instead, risk prediction for a location requires a cascade of

circumstances: a high number of asymptomatic cases frequenting the location combined with high levels of mosquitos and high numbers of people who are not immune to the particular serotype of dengue virus that is circulating.

"That's the complicated nature of this virus," Vazquez-Prokopec says. "We have underestimated the role of asymptomatic cases in spreading dengue."

Generally, about 50 to 70% of dengue cases are asymptomatic, making detection by public health officials impractical, and the current study reveals that asymptomatic cases are tied to a third of transmission.

"The lesson is that we need to focus on prevention of dengue outbreaks," Vazquez-Prokopec says. "The interventions for dengue for decades have been reactive. Simply reacting by closing a net around reported cases of the disease, however, will fail to contain an outbreak because that's missing the super spreaders."

More information: Gonzalo M Vazquez-Prokopec et al, Inapparent infections shape the transmission heterogeneity of dengue, *PNAS Nexus* (2023). DOI: 10.1093/pnasnexus/pgad024

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