Spatial Epidemiologic Analysis and Risk Factors for Nontuberculous Mycobacteria Infections, Missouri, USA, 2008–2019

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Carlos Mejia-Chew, an assistant professor in the Division of Infectious Disease at Washington University in St. Louis. We'll be discussing spatial distribution of nontuberculous mycobacteria infections and risk factors in Missouri.

Welcome, Dr. Mejia-Chew.

[Carlos Mejia-Chew] Thank you for having me in the podcast, Sarah.

[Sarah Gregory] The word 'epidemiology' has become much more part of our common lexicon since COVID, but people may not really fully understand what it is. Would you give us a brief definition?

[Carlos Mejia-Chew] Indeed, the COVID pandemic has made people more familiar with terms used in public health. The word epidemiology refers to the study of how often diseases occur in different groups of people and why.

[Sarah Gregory] Your study used spatial epidemiology. How is that different from any other kind?

[Carlos Mejia-Chew] So spatial epidemiology is a subfield of epidemiology that uses geographic information to describe health data with respect to characteristics of the population, the environment, socioeconomic factors, or other risk factors for infection to help map disease or detect clusters of disease.

[Sarah Gregory] And what is mycobacteria?

[Carlos Mejia-Chew] Mycobacteria is a type of bacteria or germ that can cause infection in different sites, but mainly affects the lung. In the lab, the waxy material of their cell walls gives them a staining property called acid fastness that is particularly important to identify them in culture samples.

[Sarah Gregory] Are there different kinds?

[Carlos Mejia-Chew] Well, clinically, the most important mycobacteria species is *Mycobacterium tuberculosis*, which causes tuberculosis in humans; but also, *Mycobacterium leprae*, which causes leprosy; and non-tuberculous mycobacteria (or NTM for short), are a diverse group of mycobacteria with over 200 species, although only a few of them can cause disease in humans.

[Sarah Gregory] Okay. Your study is specifically about nontuberculous mycobacteria. Where are they found?

[Carlos Mejia-Chew] NTMs are environmental mycobacteria. So they normally live in a wide variety of reservoirs, mainly soil and water. Their capability to live in the environment comes

from their ability to form biofilm, their adaptability to changing environmental conditions, including their resistance to disinfectants.

[Sarah Gregory] Is the incidence of it increasing worldwide or anywhere in particular?

[Carlos Mejia-Chew] So NTM infections of the lung is the most common site of disease and where most of the available epidemiological data comes from. The incidence of NTM has been reported to be increasing in many regions worldwide, including the United States, Asia (particularly South Korea, Taiwan, and Japan), and Europe. However, we don't know about other regions where there's no data available.

[Sarah Gregory] Where is it most prevalent then? Do we know?

[Carlos Mejia-Chew] Since NTM reporting is not routinely performed in most jurisdictions and is not standardized, it is difficult to compare rates of infection between countries. In the United States, the prevalence of NTM disease increased by 7.5 percent per year from 2008 to 2015, with the highest prevalence seen in those aged 65 years or older.

[Sarah Gregory] Are there different NTM species in different geographic areas?

[Carlos Mejia-Chew] That's a great question. A study from the NTM European Network done back in 2013 looked at the distribution of different NTM species in 30 countries and found differences in the geographical distribution of the species. For example, *Mycobacterium xenopi* was more common in certain European countries (like Hungary) and Canada compared to Australia and Asia. However, *Mycobacterium avium* complex (or MAC) is the predominant organism in most regions.

[Sarah Gregory] What determines which type is where?

[Carlos Mejia-Chew] So the reasons for the geographic differences in the distribution of NTM species is an area of ongoing research, but it's likely related to local climate factors or population density variations. Some studies have identified some environmental factors such as watersheds, shallower soil depth, or higher soil density to be associated with clustering of NTM infections. A study in Queensland examined the effects of climatic factors on infectious trends and found that the incidence of a particular group of NTMs increased after heavy rainfall.

[Sarah Gregory] Your study focuses on Missouri in the United States. Why?

[Carlos Mejia-Chew] Well, since I work in Washington University in St. Louis, Missouri, I started seeing an increasing number of referrals of patients with NTM infections in clinic, a lot of them with extensive pulmonary disease and coming from rural areas. So the mandatory NTM reporting surveillance that the Missouri State Health Department has provided an opportunity to look into the epidemiology and factors driving what I was seeing in clinical practice.

[Sarah Gregory] And what NTM species are found in Missouri?

[Carlos Mejia-Chew] So the most common NTM species we found in our study were *Mycobacterium avium*, *Mycobacterium fortuitum*, *Mycobacterium abscessus*, and *Mycobacterium chelonae*.

[Sarah Gregory] What time frame were you looking at?

[Carlos Mejia-Chew] We looked at all samples reported to the Missouri Department of Health and Human Services from 2008 to 2019.

[Sarah Gregory] And why did you choose that timeframe?

[Carlos Mejia-Chew] So we wanted to analyze the trend of NTM infections from the time the department of health's NTM surveillance database was established until 2019. Given the changes in delivery of healthcare services during the COVID-19 pandemic, data from 2020 onwards could have confounded the results.

[Sarah Gregory] What kinds of environmental events can increase environmental organisms?

[Carlos Mejia-Chew] So microorganisms are the most abundant and diverse organisms on Earth, and while we might not know which microbes are present in the environment, our understanding about what those microbes are actually doing in each environment and how a change in climate will impact microbial communities is really poor. However, it is thought that extreme weather and climate events such as floods, cyclones, heat waves or droughts that occur abruptly and lead to variations in temperature, humidity, or elements in the soil can have a large impact on the microbial community structure and their activity.

[Sarah Gregory] Let's talk about floods particularly. Do you know why floods increase the risk of getting these infections?

[Carlos Mejia-Chew] So the hypothesis is that extreme weather events like floods may cause disruptions in the ecosystem of these environmental mycobacteria that could lead to increase human exposure and risk for potential infection. A previous study conducted in Florida found higher numbers of hurricanes to be associated with higher numbers of NTM infections, and since hurricanes can lead to flooding, this fueled our hypothesis to look at the effect of floods on NTM infections in Missouri.

[Sarah Gregory] And who are most at risk of getting these infections?

[Carlos Mejia-Chew] In general, there are three major groups at risk. First, people with underlying lung disease like cystic fibrosis, chronic obstructive pulmonary disease, and bronchiectasis...those are at higher risk of developing NTM lung disease. Second, those who have a weakened immune system due to primary immunodeficiencies or the receipt of certain medications like chemotherapy or other medications used to treat rheumatological conditions are at risk of developing infection in the lung and outside the lung. And finally, those that suffer injuries with contaminated soil or water that contain NTMs are at risk of NTM disease outside the lung, mainly in the skin.

[Sarah Gregory] When you did your study, did you discover what types of areas are more likely to have cases—like city, rural, dry, wet?

[Carlos Mejia-Chew] Indeed, we found that the risk of NTM clustering was almost three times higher in rural counties compared to metropolitan counties, and rural is defined by the US Census Bureau as places with a population of 2,500 or fewer people. But we also found that counties with more than five flooding events per year had higher risk of NTM clustering.

[Sarah Gregory] What kind of data did you use for your study and where did you get it from?

[Carlos Mejia-Chew] So we used mandatory laboratory culture reporting from the Missouri Department of Health and Social Services surveillance system to identify NTM cases. To be included, cases needed to have one or more mycobacterial culture positive for an NTM species and have a postal code from the sample donor to be able to perform the spatial analysis.

[Sarah Gregory] Well, let's take a moment here for you to give us a brief rundown of your study.

[Carlos Mejia-Chew] We described the geographic distribution of NTM infections in the state of Missouri using data from the Missouri Department of Health surveillance system from January 1, 2008, to December 31, 2019. We used spatial statistics to detect geographic hotspots with higher-than-expected NTM infection rates and their association with sociodemographic factors and flooding events in the state.

[Sarah Gregory] So tell us what your findings were. What were the interesting things?

[Carlos Mejia-Chew] So we found that the average county NTM infection rate was 63 per 100,000 persons. Although the number of positive cultures for most types of NTM species remained stable over time, *Mycobacterium avium* did show a positive trend towards an increasing incidence, meaning that most of the increase of disease that we are seeing in Missouri is being driven by *Mycobacterium avium*. Among all NTMs detected in respiratory samples, we also... in patients with lung disease, those patients were more commonly female, older, and infected with *Mycobacterium avium*.

[Sarah Gregory] Were you surprised by anything you found?

[Carlos Mejia-Chew] Well, I think the most interesting finding we had is that counties in Missouri with more than five flooding events per year had a 38 percent higher rate of NTM infections compared to areas with no flooding. And this highlights the interplay between climate change and human disease, something that I think we are more likely to see in future.

[Sarah Gregory] What would you like public health officials to take away from your study?

[Carlos Mejia-Chew] I do think there's a need for wider public mandatory surveillance of NTM infections, as this would help us better understand NTM disease trends and the reasons behind the increased burden of disease we are seeing in clinical practice. But it would also help develop studies that focus on species-specific environmental niches to understand the subsequent transmission to humans, since this could offer relevant information to prevent infection in susceptible patients.

[Sarah Gregory] Tell us about Washington University in St. Louis, what you do there, and what your special areas of interests are.

[Carlos Mejia-Chew] I feel lucky to be at Wash. U. because it's a welcoming community that fosters research collaboration. I'm an infectious disease physician and my main area of clinical research interest is mycobacterial infections, particularly NTMs. Within NTMs, I am interested in the epidemiology, exploring risk factors for disease, but also novel therapeutics because there is still an unmet need for better treatment for NTM infections.

[Sarah Gregory] So you had mentioned something earlier about patients. Do you still see patients?

[Carlos Mejia-Chew] Yes, I see patients with NTM infections. And anecdotally, I felt like I was seeing an increased number of referrals of patients with NTMs, and that's kind of what has driven me to explore more of this disease that, to a certain degree, is kind of considered an orphan within the infectious disease realm because there's still a big need for more research in this area.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Mejia-Chew.

[Carlos Mejia-Chew] Thank you so much again for having me. It was a pleasure talking to you, Sarah.

[Sarah Gregory] And thanks for joining me out there. You can read the August 2023 article, Spatial Epidemiologic Analysis and Risk Factors for Nontuberculous Mycobacteria Infections, Missouri, USA, 2008–2019, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.