

**Epidemiology of Zika Virus in Brazil: Zika infection during pregnancy and Congenital Zika Syndrome (CZS)**

This summer I spent three months conducting research at the Laboratório Multiusuário de Apoio à Pesquisa em Nefrologia e Ciências Médicas (Multi-use Laboratory for Research Support in Nephrology and Medical Sciences) (LAMAP), at Hospital Universitário Antônio Pedro of Universidade Federal Fluminense in Niterói, a city in the state of Rio de Janeiro, Brazil.

The Riley Lab, in collaboration with Dr. Claudete Cardoso, Pediatric Infectious Diseases researcher and Associate Professor of Pediatrics at the Medical school of Universidade Federal Fluminense, had already begun a prospective cohort study of newborns with normocephaly and microcephaly whose mothers were exposed to Zika virus during pregnancy. This cohort is still being followed for cognitive and developmental abnormalities. I participated in this research group by taking on the role of a biostatistician or data manager.

Unfamiliar with the culture, the language, and the disease, my first task would become one of simple communication. I remember thinking that catching fifty percent of a conversation was an accomplishment. As a result of devoting 15 hours a week to intensive Portuguese language study under the instruction of a private teacher, English words fell out of reach and were automatically replaced with local phrases. I grew to love the language, the culture, and especially the people.

Before embarking, my understanding of the social and cultural structure of Rio, a *Cidade Maravilhosa*, was limited. I was familiar with cold statistics, how Brazil is one of the countries with the highest GINI indexes, implying vast inequality, and has one of the world's largest urban slum populations. But upon arrival I experienced a warm, vibrant city with a strong sense of identity. Locals explained to me the long history of the RJ *favelas*: how they are interconnected with the colonial past of Brazil. They seemed to be seamlessly integrated with the urban and commercial centers of the city, yet simultaneously function as their own networks to support the exploding population of Rio. The city encapsulated the incredible vibrancy and beauty while maintaining a tension with powerful gangs, violent crime, and disease.

I wanted to be there myself, to observe and understand the socio-cultural factors that might explain Zika's grip during the 2015 epidemic and today. When symptomatic cases of individuals with a mild exanthematous, fever-inducing illness sprang up in the northeastern states of Brazil, medical professionals seemed unphased. Nine months later, however, Zika became a word known around the globe, as the virus was clinically (and later confirmed in the laboratory) linked to congenital abnormalities including microcephaly, decreased brain tissue with subcortical calcifications, damage to the back of the eye, arthrogryposis, hypertonia, and other conditions. Then came the knowledge that ZIKV is potentially devastating in utero. In utero ZIKV infections are associated with a significant increase in microcephaly and other neurological and developmental abnormalities in newborns. Brazil is the epicenter of this epidemic. The country declared a national public health emergency as cases of suspected microcephaly increased, and the World Health Organization's Director-General declared ZIKV a Public Health Emergency of International Concern (PHEIC) from February to November 2016.[3] According to the most recent epidemiological bulletin from the Brazilian Ministry of Health, 17,338 probable cases of Zika fever were recorded in the country in 2017 alone, with an incidence rate of 8.4 cases/ 100 thousand inhabitants.[4] Of these, 8,703 (50.2%) were confirmed cases, and two deaths were confirmed in the laboratory.<sup>4</sup> The Brazilian national authorities

estimated the cumulative number of suspected cases of ZIKV to be 233,545 cases from 2016-2017.<sup>4</sup>

ZIKV is largely a disease of the poor, and the burden of ZIKV and CZS is particularly high among urban slum residents, which make up 22.3% of Brazil's urban population.[5] Brazil is also one of the world's most unequal countries, with a GINI coefficient of 51.3% in 2015.[6] *Favelas*, Brazil's urban slums, are defined by the UN by characteristics including insecure residential status, poor structural quality of housing, overcrowding, and inadequate access to safe water, sanitation, and other infrastructure.[7] These characteristics lead to rapid transmission of the Zika virus by creating breeding grounds for the *Aedes aegypti* mosquito, which thrives in these densely populated human settlements while wealthier residents are protected by a higher living standards and additional resources such as bed nets and air conditioning.[8]

Because the Zika epidemic began just 3 years ago, children affected by CZS still face uncertainty regarding disease progression and treatment protocol. Researchers are referring to CZS as only the tip of the Zika "iceberg," since the long-term consequences of the disease are unknown. Newborns who are unaffected at birth, born to mothers infected during pregnancy may exhibit cognitive and developmental disorders as they age, and up to 80% of those with ZIKV infection may be asymptomatic.[8] Families with a child affected by CZS also face fear and uncertainty about the disease, in addition to anxiety, isolation, depression and guilt. Considering the severity of the disease and potential for global spread, in addition to the difficulty of laboratory diagnosis and lack of an effective vaccine, I knew that CZS was and still remains a crucial and urgent topic for investigation.<sup>9</sup>

My internship was largely spent recovering, cleaning, and understanding the large amount of data that the laboratory had already collected. I had the opportunity to observe the Zika clinic days, as newborns and infants were given check-ups, physical therapy, ophthalmological and neurological exams, and medicine was prescribed to treat the babies' epileptic convulsions.

Observing the babies and all of the therapies, treatment protocols, and drug regimes that they may have to follow for life only fueled my passion for preventing new cases of congenital Zika syndrome. It raised questions. Where, when, and how do mothers become at a higher risk for having a baby with this syndrome? What measures can we put in place to prevent new cases? How can we offer support to mothers who have affected babies and who live in communities that have been historically socially and culturally marginalized? These are questions I hope to address with a combination of sound biostatistics methods and an exploration of epidemiologic strength through design.

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