Expected Increase In Microcephaly Cases In Brazil Fails To Materialize

Good News For Public Health Creates A New Epidemiologic Mystery

Despite the fact that the Zika epidemic has spread throughout Brazil since first being detected in early 2015, almost 90% of microcephaly cases have been clustered in a relatively small portion of the northeastern corner of the country where the epidemic first took off (see WHO map below). Health officials expected a similar surge in microcephaly to follow in the rest of the country, but so far that has yet to materialize.

For instance, adjacent to the areas experiencing the highest levels of microcephaly is Brazil's second-most populous state, Minas Gerais, which has reported only 3 cases of microcephaly to date. Similarly, the rest of Brazil has seen only modest increases in microcephaly despite widespread Zika transmission, leading officials to question if Zika alone is truly responsible for the large increase in severe brain abnormalities.

The Mystery

Fatima Marinho, the Brazilian Health Ministry's director of information and health analysis, recently told the Globe and Mail, "We know here Zika caused neurological damage – we have no doubt – but the question is how can we explain this situation in the epicentre that was not reproduced in other areas – in Colombia, and in other states in Brazil. A lot of pregnant women were infected and there were few cases of microcephaly or congenital malformation – it must be more than Zika itself."

Mystery In Columbia

A lot of attention is being paid to neighboring Colombia, where nearly 100,000 suspected cases of Zika have been reported since August of 2015 and as of yet there have been only 18 cases linked to birth defects. A preliminary report on the status of Zika virus in Colombia published in June in the New England Journal of Medicine found no birth defects or brain abnormalities at all in a cohort of over 600 Colombian babies whose mothers showed symptoms of Zika virus infection during their third trimester[1]. At the same time, the overall levels of microcephaly reported in Colombia have yet to show a significant increase. However, data from Brazil have shown that there is a far greater risk of birth defects from infection during the first or second trimester and the majority of the pregnant women with first and second trimester infections have not yet delivered.

New Study

Sparked by the unusual geographic distribution of microcephaly cases, the Brazilian Health Ministry is launching an official probe enlisting the help of Oliver Brady, an epidemiologist from the London School of Hygiene and Tropical Medicine, and Simon Hay, the director of geospatial science at the Institute for Health Metrics and Evaluation in Seattle. The study is aimed at identifying cofactors that may be acting in concert with Zika virus infection to produce severe birth defects.

Leading Hypotheses

The Health Ministry's new probe will explore a number of theories that may explain the high density and severity of microcephaly cases in northeastern Brazil.

1) One of the more frequently discussed hypotheses is that co-infection with another virus either before or simultaneous with Zika may alter the way the viruses interact with the mother and fetus. Both dengue and chikungunya are endemic to Brazil and some parts of the highly-affected northeastern region even experienced measles during this time period.

2) Similarly, researchers at the Federal University of Rio de Janeiro recently reported preliminary findings in an online preprint describing the discovery of bovine viral diarrhoea virus (BVDV) proteins in the brains of three fetuses with microcephaly[2]. BVDV has not been known to infect humans but causes birth defects in cattle.

3) Others have raised the possibility that socio-economic factors may play a role, as mothers of affected fetuses are overwhelmingly black or mixed-race (77% compared to52% of the total population). The majority of these women are also poor, in contrast to infection patterns of dengue which affects socio-economic classes more equally in Brazil despite being transmitted by the same mosquitos as Zika.

4) Finally, a recently published paper examined whether vaccination patterns could be a potential factor[3]. The authors found that clusters of microcephaly cases in the northeast of Brazil overlapped with areas of the lowest yellow-fever vaccination coverage in the country. The authors suggest that prior vaccination for yellow fever may convey some protection against Zika, as they are related flaviviruses. In fact, prior studies have shown that flavivirus infections can produce cross-reactive antibodies for other members of the virus family.

The Data Problem

Experts question the reliability of Brazil's data and estimates of microcephaly rates prior to the epidemic are considered inaccurate. Many believe there was overreporting of microcephaly cases once the epidemic took off and very few of these had confirmed positive lab tests for Zika. Ernesto Marques, a professor of infectious disease and microbiology at the University of Pittsburgh, summed up the situation to the Globe and Mail, "The current epidemiological info is very fragile." As part of investigating potential cofactors, an essential part of the Ministry's new probe will be a thorough reexamination of the microcephaly data itself and how it's being collected across different regions of the country.

Delay In Getting An Answer

Unfortunately, it might require time and the collection of more solid data as the epidemic spreads across South and Central America before scientists and public health officials can truly address the role of cofactors in Zika-related birth defects. Microcephaly rates in Colombia and the rest of the region over the next year should go a long way towards answering the question of whether the pattern in Brazil is a true anomaly. In addition, the Zika in Infants and Pregnancy Study is now underway in Puerto Rico tracking 10,000 pregnant women and examining a number of potential cofactors related to nutrition, environment and socio-economic status.

1. https://tinyurl.com/z7bz5lj
2. https://tinyurl.com/zlcmhls
3. https://tinyurl.com/hgo5tvh

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