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TAILING A VIRUS

Relevant for: Developmental Issues | Topic: Health & Sanitation and related issues

It is a time of peace and quiet for India on the Zika front. Madhya Pradesh and Rajasthan, which saw large outbreaks late last year, stopped seeing new cases before the year end. For health authorities, the temptation may be to consider the threat past, and move on to more pressing concerns, like the large number of H1N1 influenza cases this year. The truth, however, is that this is an excellent time to study Zika epidemiology in India. Public health officials must do this while disseminating data quickly and transparently, so that it can be analysed by the global scientific community. This is in India's best interests.

What are the data that health authorities should be collecting? First, they must leave no stone unturned in following up on every pregnant woman who was diagnosed Zika positive in Rajasthan and Madhya Pradesh. When the epidemics began, there were worrying indications that Central and State health officials were downplaying the risk to pregnant women. Even though there is no evidence conclusively linking a particular viral strain or mutation with foetal anomalies, the Indian Council of Medical Research (ICMR) said the Rajasthan strain did not have the S139N mutation linked to microcephaly.

This is incorrect. Even though microcephaly was first observed as a consequence of Zika during the 2015 Brazilian epidemic, strains other than the Brazilian strain, which do not have the S139N mutation, have been linked with the abnormality. For example, in 2017, when the virus from a foetus with microcephaly in Thailand was sequenced, it did not have the S139N mutation. Researchers also showed that a 1966 Malaysian virus strain — isolated long before Zika was seen to cause microcephaly in Brazil — was as effective at infecting foetal mouse brains as the Brazilian one. In another 2017 study, published in *Development*, a strain from the African virus lineage, which was hitherto not thought to cause microcephaly, was seen to be more damaging to mouse brains than the Asian lineage (to which the Brazilian strain belongs).Given this research, we must assume that all Zika strains can cause microcephaly.

If this is the case, why did the link between microcephaly and Zika become evident only in the 2015 Latin American epidemic? Prior to this, numerous outbreaks had occurred in Southeast Asia. Yet, no one picked up on this phenomenon. Scientists have proposed several explanations for this mystery. One is that Zika has always caused microcephaly, although the link became obvious only in Brazil because so many people were infected. Another possibility is that poverty and malnutrition worsen the progression of the disease in pregnant women. This would explain why northeast Brazil, with its widespread poverty, was the most severely affected by microcephaly. Scientists are also probing whether simultaneous infection with dengue or chikungunya make the children of Zika-infected women more prone to foetal anomalies. Two studies published earlier this year show conflicting evidence for the role of dengue. The first, published in *Immunity*, showed that in mice, the presence of dengue antibodies led to more placental damage and restricted foetal growth due to Zika. Another study in *Science* showed that people infected by dengue were protected against Zika during an outbreak in Salvador, Brazil.

Given this conflicting evidence, scientists are very far from understanding what makes Zika deadly to foetuses. This means that any data on how the pregnancies of Zika-infected women pan out in India can be enlightening. Careful studies must be carried out to see if there is increased prevalence of microcephaly, and to understand the risk-factors. Already, the TORCH (Toxoplasmosis, Other, Rubella, Cytomegalovirus, and Herpes) infections are known to cause foetal abnormalities, including microcephaly, among newborns. Wherever women are screened

for TORCH, they must also be screened for Zika.

It's also important to remember that the Zika risk doesn't end after the baby is born healthy. The experience of Latin America showed that even healthy newborns can go on to develop symptoms later. This has led to estimates of the incidence of birth defects being revised upwards.

The other important bit of actionable information that health authorities can and should gather concerns population immunity. To study immunity, authorities must conduct seroprevalence surveys, in which they screen people in several States for antibodies to zika. Many Indians could well have such antibodies, which means they are protected to some extent. The reason they are likely to have antibodies is because the Rajasthan outbreak virus was around in the State since at least 2016. Moreover, as a recent paper by researchers from the National Institute of Virology revealed, the Rajasthan strain is endemic to Asia, which means it could have been in India for decades now. Still, exposure to the virus does not guarantee a lifetime of protection. So, seroprevalence surveys are needed to identify pockets of low immunity in India. Health authorities can then focus their efforts on these regions, because they would be most vulnerable to future outbreaks.

It is true that seroprevalence studies are not easy to do, given the cross-reactivity that plagues flaviviruses. The Enzyme-linked immunosorbent Assay (ELISA), which is commonly used in seroprevalence studies to detect antibodies, can throw up false positives for Zika if a person has dengue antibodies. This is because dengue antibodies can neutralise Zika and vice versa.

The good news is that researchers are working to develop alternative tests that are specific to Zika alone. One multinational team, including Swiss firm Humabs BioMed, has developed an ELISA test that is able to distinguish Zika from dengue. The test was used in a survey at Managua, Nicaragua after a large epidemic hit the city in 2016. It found that in 2017, 56% of tested adults had antibodies to Zika, suggesting that the city wouldn't see another large epidemic in the near future. India should consider doing such surveys too.

The outbreaks in Rajasthan and Madhya Pradesh have seemingly ended, which is good news. But given that the virus is already in these States, and these States have well connected transportation links, there is reason to expect future outbreaks when the mosquito season begins again. Outbreak response should not end when an outbreak ends, because that is when efforts to contain the next epidemic begin. If India is lucky, the next epidemic will not be a big one. But it is not an assumption that health authorities should make.

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