

# NEWS IN FOCUS

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UESLEI MARCELINO/REUTERS



Mothers of children with suspected microcephaly await medical care at a hospital in Recife, Brazil.

## ZIKA VIRUS

# Microcephaly surge in doubt

*Heightened awareness of Zika virus could help to explain the reported spike in birth defects.*

BY DECLAN BUTLER

**A**s alarm grows about the rapid spread of the Zika virus through the Americas, researchers are questioning the extent of an apparent surge in Brazil of microcephaly — a birth defect in which babies are born with abnormally small heads and brains — which has been tentatively linked to the virus.

On 1 February, the possibility that microcephaly is linked to Zika prompted the World Health Organization (WHO) to label the situation a “public health emergency of

international concern”, a mechanism that will allow it to coordinate an international response, among other things.

But Jorge Lopez-Camelo and Ieda Maria Orioli, from the Latin American Collaborative Study of Congenital Malformations (ECLAMC), say that a rise in reported cases of microcephaly might largely be attributable to the intense search for cases of the birth defect and to misdiagnoses, arising from heightened awareness in the wake of the possible link with Zika.

The ‘awareness’ effect is well known and

inevitable, they say, and must be revealing cases that would have gone unnoticed under normal circumstances. And a high rate of misdiagnoses among reported cases of microcephaly is likely because the diagnostic criteria being used are broad. Lopez-Camelo and Orioli posted their analysis on the ECLAMC website in Portuguese, and, after *Nature's* enquiries, provided an English-language version of the summary (see [go.nature.com/v77ntu](http://go.nature.com/v77ntu)).

They say that from the epidemiological data available, it is impossible to establish the ▶

► true size of the surge in microcephaly, and whether there is any link with the Zika virus.

In particular, large prospective studies are needed, in which pregnant women in areas of Brazil experiencing Zika outbreaks would be monitored to see how many of their children develop microcephaly, say Lopez-Camelo and Orioli. Several research groups in and outside Brazil are already planning such studies, and some have begun.

Specialists contacted by *Nature* emphasize that pregnant women should still be cautious — for example, by protecting themselves against mosquito bites — until more is known.

These experts agree with the ECLAMC team that the reported size of the microcephaly increase so far is probably inflated — but some disagree with the further conclusion that the reported rise is mostly an artefact.

Thomas Jaenisch, a tropical-medicine specialist at the Heidelberg University Hospital in Germany, calls the attribution of most of the surge to these awareness effects an “extreme” position, and says that it “might also create uncertainty in the media and public discussion in Brazil”.

On 27 January, the Brazilian government said that of 4,180 suspected microcephaly cases recorded since October, it has so far confirmed 270 and rejected 462 as false diagnoses.

Previously confined to Africa and Asia, Zika virus reached the Americas in 2015, where it is now causing an unprecedented epidemic in Brazil and outbreaks in several countries (see ‘Zika in the Americas’). Most people infected with the virus — after being bitten by a mosquito — have no symptoms. The remainder have mild symptoms such as fever, skin rash and headache.

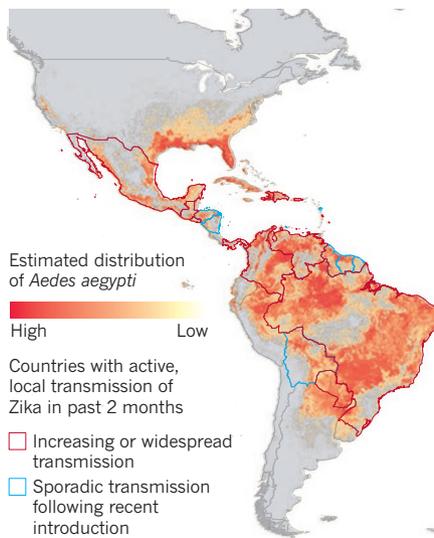
But in October, Brazil’s health ministry reported an unusual spike in reported cases of microcephaly in the northeastern state of Pernambuco, where the affected children’s mothers had been in early pregnancy at around the same time as large Zika outbreaks occurred. The ministry subsequently raised the alarm of a possible link to Zika.

This led the WHO and its regional office, the Pan American Health Organization, to issue an epidemiological alert on 17 November, which called on member states to look for any similar increase in microcephaly among their populations.

To investigate, the researchers at the

## ZIKA IN THE AMERICAS

Following its arrival in the Americas in 2015, Zika virus is now being actively transmitted in many of the countries that harbour its main carrier, the *Aedes aegypti* mosquito.



ECLAMC turned to its own databases dating back to 1967, as well as the country’s Live Birth Information System (SINASC).

According to the ECLAMC, the average historical prevalence of microcephaly in Brazil is around 2 cases per 10,000 births, although rates in the country’s north have typically been higher. The researchers calculate that the maximum number of cases that would have been expected in the northern state of Pernambuco in 2015 is around 45. Yet Pernambuco reported 26 times that number last year. Even if Zika is causing microcephaly, these huge numbers are simply too high to be credible, says the report.

## INCREASED SURVEILLANCE

As well as the increased diagnoses resulting from heightened awareness, Lopez-Camelo also highlights that the diagnostic criteria for microcephaly are relatively unspecific and cast too wide a net. Brazilian health authorities are treating all fetuses with head circumferences that are more than two standard deviations below the average, and newborns with a head circumference of less than 32 centimetres, as suspected cases. But these criteria will inevitably capture many healthy children within the normal growth range who do not have

microcephaly. And head circumference is only a proxy measure, note Lopez-Camelo and Orioli: confirming microcephaly requires a diagnosis of small brain size, and a decreased rate of brain growth.

A risk assessment published on 21 January by the European Centre for Disease Prevention and Control also noted the broad diagnostic criteria and said: “It is expected that many of the suspected cases will be reclassified and discarded.”

The ECLAMC’s conclusion — that the apparent surge could be largely an artefact — is possible in principle, says Helen Dolk, an epidemiologist at the University of Ulster near Belfast, UK, who works on the surveillance of congenital abnormalities. But she stresses that it is impossible to confirm until more data become available — and that she is reserving judgement on the portion of the apparent increase that can be attributed to confounding factors.

## REAL CONCERN

By contrast, Lavinia Schüler-Faccini, a researcher at the Federal University of Rio Grande do Sul, and president of the Brazilian Society of Medical Genetics, says she is certain that there has been a substantial increase in microcephaly cases. She notes that physicians began reporting a rise before the increased attention by health authorities, and the media began reporting a spike last November. “My personal impression is that there is an augmentation of cases of microcephaly in Brazil,” she says, but adds that it is not as huge as the suspected number of cases reported to the health ministry. “All our efforts now are to establish the real level of increase.”

Establishing whether there is a link between microcephaly and Zika is particularly important because people living in the Americas lack immunity to the virus. This, combined with the fact that the *Aedes* mosquitoes that transmit Zika are widespread in the Americas, means that many people will be infected in future, including pregnant women.

Zika virus has been found in amniotic fluid, placental or fetal tissues in several cases of nervous-system malformations, including microcephaly, in Brazil. In a 1 February statement, the WHO said: “A causal relationship between Zika infection during pregnancy and microcephaly is strongly suspected, though not yet scientifically proven.” ■ SEE EDITORIAL P.5

SOURCE: ECDC (ZIKA-TRANSMISSION DATA); M. U. G. KRÄEMER ET AL. *ELIFE* 4, E08347, 2015 (MOSQUITO RANGE)

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**CORRECTION**

The two elements in the key for the map in the News story 'Microcephaly surge in doubt' (*Nature* **530**, 13–14; 2015) were accidentally swapped round. The corrected graphic can be seen at [go.nature.com/ekmksk](http://go.nature.com/ekmksk).