

New evidence suggests Zika virus can cross placental barrier, but link with microcephaly remains unclear

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Transmission electron micrograph (TEM) of Zika virus. Credit: Cynthia Goldsmith/Centers for Disease Control and Prevention

Zika virus has been detected in the amniotic fluid of two pregnant



women whose foetuses had been diagnosed with microcephaly, according to a study published today in *The Lancet Infectious Diseases*. The report suggests that Zika virus can cross the placental barrier, but does not prove that the virus causes microcephaly, as more research is needed to understand the link.

Researchers also analysed the whole genome of the <u>virus</u> found in the two <u>pregnant women</u> and confirmed that the virus is genetically related to the strain identified during an outbreak of Zika virus in French Polynesia in 2013.

"Previous studies have identified Zika virus in the saliva, breast milk and urine of mothers and their newborn babies, after having given birth. This study reports details of the Zika virus being identified directly in the <u>amniotic fluid</u> of a woman during her pregnancy, suggesting that the virus could cross the placental barrier and potentially infect the foetus" said Dr Ana de Filippis, lead author from the Oswaldo Cruz Institute in Rio de Janeiro, Brazil.

The placental barrier is made up of layers of tissue in the placenta and regulates the exchange of substances (including infections) between the mother and foetus. The amniotic fluid is the protective liquid around the foetus.

Dr de Filippis added "This study cannot determine whether the Zika virus identified in these two cases was the cause of microcephaly in the babies. Until we understand the biological mechanism linking Zika virus to microcephaly we cannot be certain that one causes the other, and further research is urgently needed."

The number of reported cases of newborn babies with microcephaly in Brazil in 2015 has increased twenty-fold compared with previous years. At the same time, Brazil has reported a high number of Zika virus



infections, leading to speculation that the two may be linked. Babies born with microcephaly have abnormally small heads, and are at risk of incomplete brain development. Microcephaly has previously been linked to a range of factors including genetic disorders, drug or chemical intoxication, maternal malnutrition and infections with viruses or bacteria that can cross the placental barrier such as herpes, HIV, or some mosquito borne viruses such as chikungunya.

In this study, the team led by Dr de Filippis investigated the case of two women (aged 27 and 35) from Paraiba, a state in northeast Brazil. The two women presented with symptoms of Zika virus infection including fever, muscle pain and a rash during their first trimester of pregnancy. Ultrasounds taken at approximately 22 weeks of pregnancy confirmed the foetuses had microcephaly.

Samples of amniotic fluid were taken at 28 weeks of pregnancy and analysed for potential infections. Both patients tested negative for dengue virus, chikungunya virus and other infections such as HIV, syphilis and herpes. Although the two women's blood and urine samples tested negative for Zika virus, their amniotic fluid tested positive for Zika virus genome and Zika antibodies. The amniotic fluid was analysed using a process called metagenomic analysis. This allows the detection of any microorganism that could be present in the samples, but only Zika virus genome was found. The RNA of the two Zika virus samples was then compared with samples from previous outbreaks, and was found to be genetically related to the strain identified in French Polynesia in 2013.

Writing in a linked Comment, Professor Didier Musso from the Unit of Emerging Infectious Diseases, Institut Louis Malarde in Tahiti, French Polynesia, says: "Even if all these data strongly suggest that Zika virus can cause microcephaly, the number of microcephaly cases related to Zika virus is still unknown. The next step will be to do case-control



studies to estimate the potential risk of microcephaly after Zika virus infection during pregnancy, other fetal or neonatal complications, and long-term outcomes for infected symptomatic and asymptomatic neonates."

More information: *The Lancet Infectious Diseases*, <u>www.thelancet.com/journals/lan ... (16)00095-5/abstract</u>

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