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# Correspondence

## Ascertaining fetal Zika virus infection based on IgM antibody test in endemic settings

We read with interest the article by Pomar *et al.*[1] on the association between Zika virus and fetopathy in a French Guianese population. This observational study raises some issues that we feel should be brought to the readers' attention.

First, the authors' rationale to include a Zika virus (ZIKV)-specific IgM antibody test as part of the positive case definition, despite the test's cross-reactivity with other Flavivirus infections and immunizations, is not clear. As described previously[2], the levels of anti-ZIKV IgM may appear elevated as a result of antibody cross-reaction among viruses of the same family. A false-positive result could therefore lead to misdiagnosis of an otherwise normal fetus. The International Society of Ultrasound in Obstetrics and Gynecology recommends the use of reverse transcription polymerase chain reaction (RT-PCR) or consultation with an expert when interpreting ZIKV IgM positive results[3]. For example, studies in endemic populations in Colombia and Brazil did not include detection of ZIKV IgM antibodies for defining a positive case and instead used only RT-PCR assays[4,5]. Consequently, suggesting that a test for ZIKV IgM antibody alone is sufficient for diagnosing ZIKV would affect outcomes of clinical practice in endemic settings.

Second, the authors did not report the results of karyotype or chromosomal microarray following amniocentesis. For example, in the data provided for Case 6 (a twin pregnancy), the mother tested positive for serum anti-ZIKV IgM/IgG and for serum RT-PCR ZIKV but ZIKV was not found in fetal tissues. This raises the question of whether the central nervous system abnormalities identified in Fetus A could be attributed to chromosomal or microdeletion abnormalities[6]. The same argument could be made for Case 9, a case of non-immune hydrops fetalis that showed negative ZIKV RT-PCR of the placenta and fetal tissues. In this scenario, calculating the vertical transmission rate of ZIKV could provide a misleading interpretation.

Third, it is unclear whether or not the authors investigated other maternal comorbidities, such as pre-eclampsia, obesity and pregestational diabetes; the authors reported vascular risk as the sole cofactor. Moreover, the authors did not provide further explanation of the contribution to the outcomes from these vascular risk factors.

We acknowledge that the authors implemented changes to the definition of microcephaly used by the Centers for Disease Control and Prevention and the World Health Organization to decrease the number of false positives[3,6,7]. Also, we welcome their findings that the risk of microcephaly did not differ for the ZIKV-exposed and non-exposed groups. We also agree that detailed neurosonography is the method of choice for follow-up in exposed subjects. However, as medical providers, we need to understand that the accuracy of the available laboratory tests to identify fetal infection remains low. We can address this limitation by performing neurosonography, close postnatal follow-up and clinical examination. Such strategies should limit the extent of this outbreak and improve prognosis of the neonatal population.

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