Title

Kinetics of anti-Zika virus antibodies after acute infection in pregnant women

Authors

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The kinetics of anti-Zika virus (ZIKV) antibodies after acute ZIKV infection is not well known (1,2), especially in areas where different flaviviruses circulate (3). The objective of this study was to describe the kinetics of anti-ZIKV antibodies in women in whom an acute ZIKV infection was diagnosed during pregnancy. Within a cohort of pregnant women living in Guadeloupe and exposed to ZIKV during the 2016 Zika outbreak (4), we identified 65 women who presented with an acute, symptomatic, PCR-confirmed (RealStar Zika Virus RT-PCR Kit 1.0, Altona Diagnostics) ZIKV infection at various times of their pregnancy, with a known date of first Zika symptoms. Serum samples obtained at delivery in all women and at various interim timepoints between acute ZIKV infection and delivery in 20 women (23 samples) were tested for anti-ZIKV antibodies. The 88 serum samples were batch processed, using the commercially available ELISA Euroimmun® assay (5,6) and a Virus Neutralisation Test (VNT) that was performed at the French National Reference Center for Arboviruses (7) in order to detect anti-ZIKV IgM and IgG antibodies and confirm the presence of anti-ZIKV neutralizing antibodies, respectively. Moreover, a Dengue virus (DENV) ELISA assay was performed on all samples.

Patients’ mean age was 30 years. Time between first symptoms of ZIKV infection and delivery ranged from 17 to 229 days. Mean time between ZIKV infection and delivery was 197, 119, and 50 days for women who had acute ZIKV infection during 1st (n=14), 2nd (n=35), and 3rd (n=16) trimester of pregnancy, respectively. DENV serology was positive in all women. ZIKV serology on delivery samples was positive in 65/65 (100%; one-sided 97.5% CI: 94.4%-100%) women by both IgG ELISA and VNT assays. IgM anti-ZIKV antibodies were detected as early as 2 days after first symptom and progressively faded away over a few weeks. They were detected on delivery samples in only 5/65 (8%) women, in whom time intervals between acute ZIKV infection and sampling were 17, 27, 36, 38, and 142 days. IgG anti-ZIKV
antibodies were negative in all 6 interim samples that had been drawn within 7 days of first symptom. They were detected from Day 13 and remained positive afterwards. The kinetics of anti-ZIKV antibodies is summarized in the Figure.

The main finding of this study is that with the Euroimmun® assay, IgG anti-ZIKV antibodies were detected as early as the second week after acute ZIKV infection and remained detectable until delivery in all women.

The strengths of this study are two-fold: 1) the kinetics of antibodies could be established because the date of acute ZIKV infection was ascertained by the combination of consistent clinical symptoms and concomitant positive nucleic acid testing; and 2) the antibodies detected by Euroimmun® ELISA assay were specific to ZIKV, as evidenced by the results of a seroneutralization assay. The main limitation of this study results from the small number of serum samples that were drawn between acute infection and delivery. However, these numbers were in the same range as those in two comparable studies that showed results similar to ours regarding the kinetics of anti-ZIKV IgG antibodies (1,2).

Altogether, the pragmatic interpretation of our findings is that the absence of IgG anti-ZIKV antibodies at delivery appears to be a strong indicator of the absence of ZIKV infection during pregnancy, an information that is quite useful to inform pregnant women on the potential risks for their neonates.
**Funding**

This study was funded by the French Ministry of Health (Soutien Exceptionnel à la Recherche et à l'Innovation) and by the European Union’s Horizon 2020 Research and Innovation Programme under ZIKAlliance Grant Agreement no. 734548.

**Acknowledgments**

We thank the women who participated in this study and acknowledge their altruism. We want to acknowledge all actors (physicians, midwives, clinical research assistants, health officers and epidemiologists) who joined their efforts to help conduct this study. We are grateful to Joelle Colat-Peyron for handling serology testing at Karubiotec.
References


Figure: Kinetics of anti-ZIKV antibodies in the 88 samples tested in 65 pregnant women.

Notes:

Times intervals are between day of first Zika symptom and day of blood sampling. Five women delivered within 2 months of acute ZIKV infection, which explains why only 60 samples were available in the interval 'After 62 days'.