

# Anti-Zika virus IgA may indicate an acute infection in anti-Zika virus IgM-negative patients

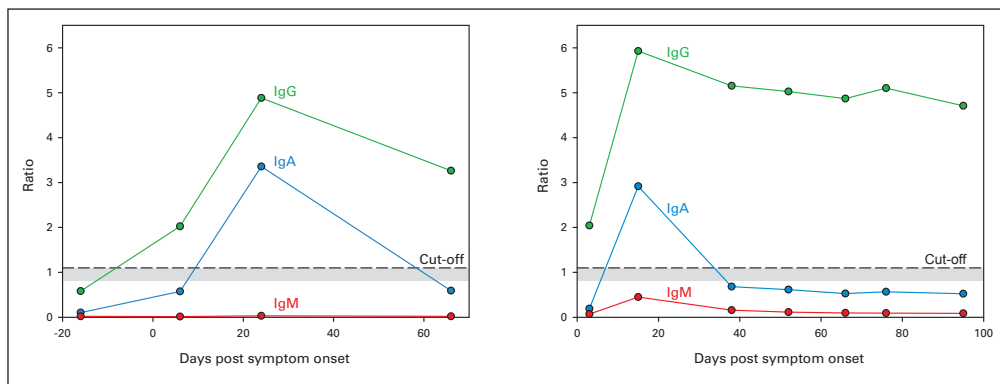
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Patient	Country of origin	Country of infection	Days after symptoms	Anti-ZIKV IgA ratio; pos: $\geq 1.1$	Anti-ZIKV IgM ratio; pos: $\geq 1.1$	Anti-ZIKV IgG ratio; pos: $\geq 1.1$
1	Colombia	Colombia	-16	0.1	0.0	0.6
			6	0.6	0.0	2.0
			24	3.4	0.0	4.9
			66	0.6	0.0	3.3
			66	0.6	0.0	3.3
2	Colombia	Colombia	3	0.2	0.1	2.0
			15	2.9	0.5	5.9
			38	0.7	0.2	5.2
			52	0.6	0.1	5.0
			66	0.5	0.1	4.9
			76	0.6	0.1	5.1
			95	0.5	0.1	4.7
3	Germany	Martinique	11	4.1	1.0	0.1
			16	9.0	2.7	1.4
			36	1.5	1.2	2.5
			36	1.5	1.2	2.5
4	Germany	Nicaragua	4	0.3	0.2	0.2
			9	7.6	2.4	1.0
			30	2.4	0.9	3.0

## Introduction

In secondary flavivirus infections, specific IgM is often found at low or undetectable titers, while synthesis of specific IgG is rapidly stimulated. Shortly after infection the IgG titer levels off being indistinguishable from IgG titers in convalescent infections. The same has been observed in patients with **Zika virus (ZIKV)** infections from regions endemic for other flaviviruses. Since ZIKV infection is suspected to be associated with major neurological consequences, differentiation between acute (secondary) and past infections is crucial. We analysed the course of anti-ZIKV IgA, IgM and IgG titers in sequential serum samples of four patients, investigating whether IgA might indicate an acute phase of infection.

## Methods

Serum samples were taken at several time points from two Colombians with a presumptive background of past flavivirus infections and from two German travellers, all presenting with confirmed ZIKV infections.

Titers of anti-ZIKV IgM and IgG were measured using a commercial NS1-based Anti-Zika virus ELISA (cut-off  $\geq 1.1$ , Euroimmun AG, Germany). An indirect immunofluorescence test (Arbovirus Fever Mosaic 2, IgM, cut-off  $\geq 1:10$ , Euroimmun AG, Germany) based on cells infected with ZIKV was used additionally for IgM measurement. For determination of anti-ZIKV IgA, the ELISA was adapted, applying an anti-

human IgA conjugated with peroxidase. The cut-off was set to a ratio of 1.1.

## Results

In the German travellers, anti-ZIKV IgM was detected with ELISA as well as IIFT at day 9 and day 16, respectively. Active infections were confirmed by subsequent anti-ZIKV IgG seroconversion. Anti-ZIKV IgA measurements were above 1.1 in all samples except for one, showing an initial increase and a subsequent decrease.

In the sequential samples of the Colombian patients, measurements of IgM antibodies against ZIKV-NS1 antigen in ELISA were

persistently below the cut-off. In accordance, testing for IgM against full ZIKV in IIFT was negative in all but one, weak positive sample (1:10). Anti-ZIKV IgG was positive already within the first week in both patients. IgA, however, showed a titer increase, peaking above the cut-off in week three and four before dropping below the threshold again.

## Conclusion

When specific IgM is not detectable neither with NS1- nor full virus-based assays as observed in the Colombian patients, measurement of anti-ZIKV IgA may allow discrimination of acute from past infections.