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Testing anti-Zika virus NS1 IgA additionally to IgM increases sensitivity in acutely infected patients from regions endemic for flaviviruses

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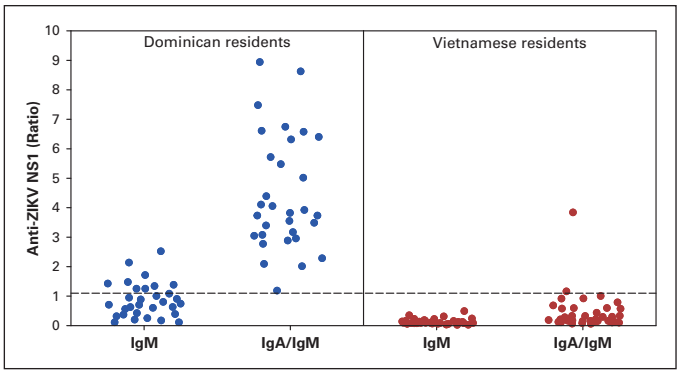
Panel	n	Anti-Zika virus NS1 ELISA		
		Result	IgM	IgA/IgM
Dominican residents with acute ZIKV infection	31	positive	9	31
		negative	22	0
Sensitivity	31		29.0 %	100 %
Vietnamese residents with acute DENV infection	40	positive	0	2
		negative	40	38
Specificity	40		100 %	95.0 %

Diagnostic performance of the NS1-based anti-Zika virus ELISA (Euroimmun) for the combined detection of virus-specific IgA/IgM compared to IgM only



Anti-ZIKV NS1 IgM vs. IgA/IgM reactivity in Dominican patients with acute ZIKV infection compared to DENV-infected Vietnamese controls

Introduction

Specific IgM response to **Zika virus (ZIKV)** can be low or absent in patients with acute ZIKV infection and a history of other infections with related flaviviruses, e.g. **dengue virus (DENV)**, presenting with an early high IgG titer. In these ZIKV cases, IgA against ZIKV **non-structural protein 1 (NS1)** was observed in the acute phase, suggesting anti-ZIKV IgA as alternative acute marker in secondary infections. In this study, we investigated the diagnostic benefit of an ELISA for combined detection of anti-ZIKV NS1 IgA and IgM.

Methods

The following human serum panels were included in this study:
1) A sensitivity panel (panel 1) comprising acute serum samples (day 8-16 post symptom onset) of 31 residents from the Dominican Republic (2015), where ZIKV and DENV are endemic. Patients had been tested positive for ZIKV nucleic acid and anti-DENV IgG during the viraemic phase (≤day 5).

2) A specificity panel (panel 2) consisting of serum samples (day 3-7 post symptom onset) of 40 Vietnamese patients, hospitalised with DENV haemorrhagic fever according to the World Health Organization case definition grade I and tested positive for DENV nucleic acid and anti-DENV IgG. Vietnam (2015) is endemic for DENV but not for ZIKV.

Anti-ZIKV NS1 antibodies were determined in each sample using a commercial NS1-based Anti-Zika virus ELISA IgM (Euroimmun AG, Germany) and a corresponding ELISA (Euroimmun), applying a combination of anti-human IgA/IgM conjugated with peroxidase.

Results

In panel 1, 29 % (9/31) of samples were positive for anti-ZIKV NS1 IgM, whereas 100 % were positive for combined specific IgA and IgM. In panel 2, none of the sera reacted in the Anti-Zika virus ELISA IgM, two samples were reactive in the Anti-Zika virus IgAM ELISA (5.0 %).

Conclusion

Since patients with acute ZIKV infection from flavivirus endemic regions may not develop NS1-specific antibodies of class IgM, additional testing of anti-ZIKV NS1 IgA is required.

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