Comparison of Two Zika IgM Antibody Capture Enzyme Linked Immunosorbent Assays (MAC-ELISA) in Symptomatic Patients from Dominican Republic, 2016

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Background: Zika virus (ZIKV) is a *Flavivirus* transmitted to humans by *Aedes* mosquitos. To assess the clinical presentation in 434 symptomatic patients (64 men, 370 women [65 pregnant; 305 nonpregnant]) during a ZIKV outbreak in the Dominican Republic (DR) in 2016, we evaluated clinical symptoms, ZIKV by qualitative detection of ZIKV RNA and ZIKV IgM by two MAC-ELISA assays, one from CDC and performed by the Florida Department of Health, Jacksonville, FL and one from InBios International Inc., Seattle, WA (Zika Virus Detect).

Methods: The Aptima ZIKV assay (Hologic, San Diego, CA) was used to detect ZIKV by transcription-mediated amplification RT-PCR in serum, plasma or urine. Corresponding clinical symptomology reports were reviewed for all 434 patients. The results from the two MAC-ELISA assays were evaluated by linear regression analysis. The two MAC-ELISA assays were reported as optical density (OD) ratios from a sample with three different antigens (P/N ratio for CDC Zika MAC-ELISA and Zika Immune Status Ratio or ISR for InBios Zika Virus Detect MAC-ELISA).

Results: There was a biphasic increase in ZIKV detection in April and late May/June 2016 in the 434 symptomatic patients. All 434 had one or more of four symptoms including rash, fever, conjunctivitis and arthralgia.

First ZIKV NAT Positive for 434 Symptomatic Males and Females, Domincan Republic, 2016
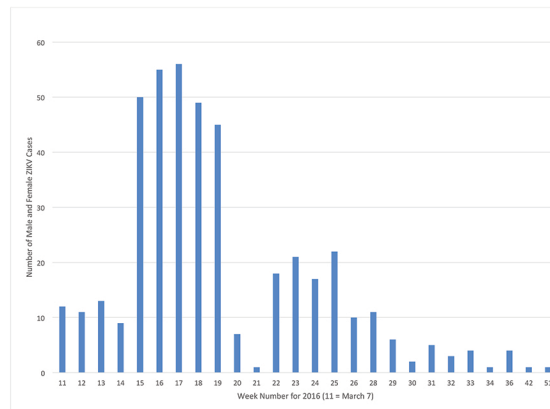
Linear regression analysis (log scale) of results from subject samples tested on the two MAC-ELISAs (282 total) revealed a slope of 1.172, y intercept of 0.1584 and R² of 0.587.

Zika IgM CDC MAC-ELISA and InBios MAC-ELISA Tested in 282 Pateients (log scale)

$$y = 1.172x + 0.1584$$
$$R^2 = 0.587$$
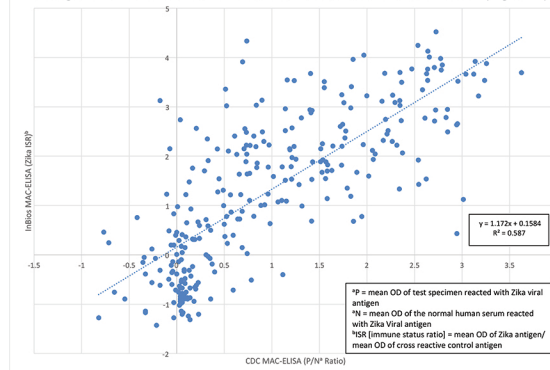
In 88 RT-PCR negative patients, 48 (54.5%) were positive by both MAC-ELISAs; 27 (30.7%) were negative by both MAC-ELISAs and 13 (14.7%) had discrepant results with a sensitivity of 85% for the InBios MAC-ELISA. The InBios also detected IgM in 54.4% of samples that were positive for ZIKV by RT-PCR attributable to errors in determining the days post symptom onset.

CDC MAC and InBios MAC Results

Table 1. Results Distribution for 88 RT-PCR Neg. Patients*

CDC MAC	InBios MAC	RT-PCR Neg.
Pos.	Pos.	48 (54.5%)
Neg.	Neg.	27 (30.7%)
Pos.	Neg.	4 (4.5%)
Neg.	Pos.	2 (2.3%)
Eq.	Pos.	4 (4.5%)
Eq.	Neg.	1 (1.1%)
Neg.	OF	1 (1.1%)
Pos.	OF	1 (1.1%)

Table 2. Results Distribution for 193 RT-PCR Pos. Patients*

CDC MAC	InBios MAC	RT-PCR Pos.
Pos.	Pos.	89 (46.1%)
Neg.	Neg.	67 (34.7%)
Pos.	Neg.	12 (6.2%)
Neg.	Pos.	9 (4.7%)
Eq.	Pos.	7 (3.6%)
Eq.	Neg.	4 (2.1%)
Neg.	OF	2 (1%)
Eq.	OF	2 (1%)
Pos.	OF	1 (0.5%)

* See appropriate supporting database.

Conclusions: In 2016 there was a biphasic spike of ZIKV positive infections in 434 symptomatic men and women tested in DR. Both linear regression analysis and our comparative analysis in the ZIKV RT-PCR positive and negative cohorts demonstrate that the InBios Zika Virus Detect MAC-ELISA provides diagnostic results comparable to the CDC Zika MAC-ELISA.