The Asian Zika Virus in Singapore does not cause false positives with the SD Dengue NS1+Ab Combo Assay

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BACKGROUND

Zika Virus & Dengue Virus
Both spread by *Aedes aegypti*
Co-circulate in many countries

And Both cuse a mild illness in most patients
Specific therapy is not available

So Distinguishing and specifying these two infections has had little clinical relevance

RECENTLY

Zika Virus is neurotropic
Early data show the incidence of microcephaly may be 1% for if infected in the 1st trimester.

CONCERN

Pregnancies infected later in gestation
May be affected
More subtle but serious defects

CONSEQUENCE

A worried pregnant woman may request
To have multiple serial tests for ZikaV
To test partners for ZikaV

An infected pregnant woman may request
Serial ultrasounds
Consider termination

For this reason it is now more desirable to distinguish ZikaV from DenV and other causes of similar clinical syndromes.

More emphasis on a correct diagnosis
Antibody assays show cross reactivity
Precise diagnosis is often difficult, unless the patient presents in early illness and PCR is available

EXISTING DATA

Dengue NS1 antigen might cross react with ZikaV
Ref; False positive dengue NS1 antigen test in a traveller with an acute Zika virus infection imported into Switzerland. Swiss Med Wkly. 2016;146:w14296.

AIM

Dengue is endemic in Singapore. An outbreak of ZikaV in August 2016 gave us the opportunity to assess the routine Dengue NS1 assay for false positives due to ZikaV infection.

MATERIALS AND METHODS

Audit of data at Tan Tock Seng Hospital, Singapore
Records of patients with both
positive 'in-house' ZikaV rt-PCR
& a DenV NS1 antigen test performed

ZikaV rt-PCR EID 2008 14,8; 1232 -1239.
NS1 assay (Alere) SD Dengue NS1+Ab Combo Assay, reports NS1 & anti-Dengue IgM and IgG

Samples positive for ZikaV and Dengue NS1 were tested with the CDC DENV-1-4 Real-Time rt-PCR assay

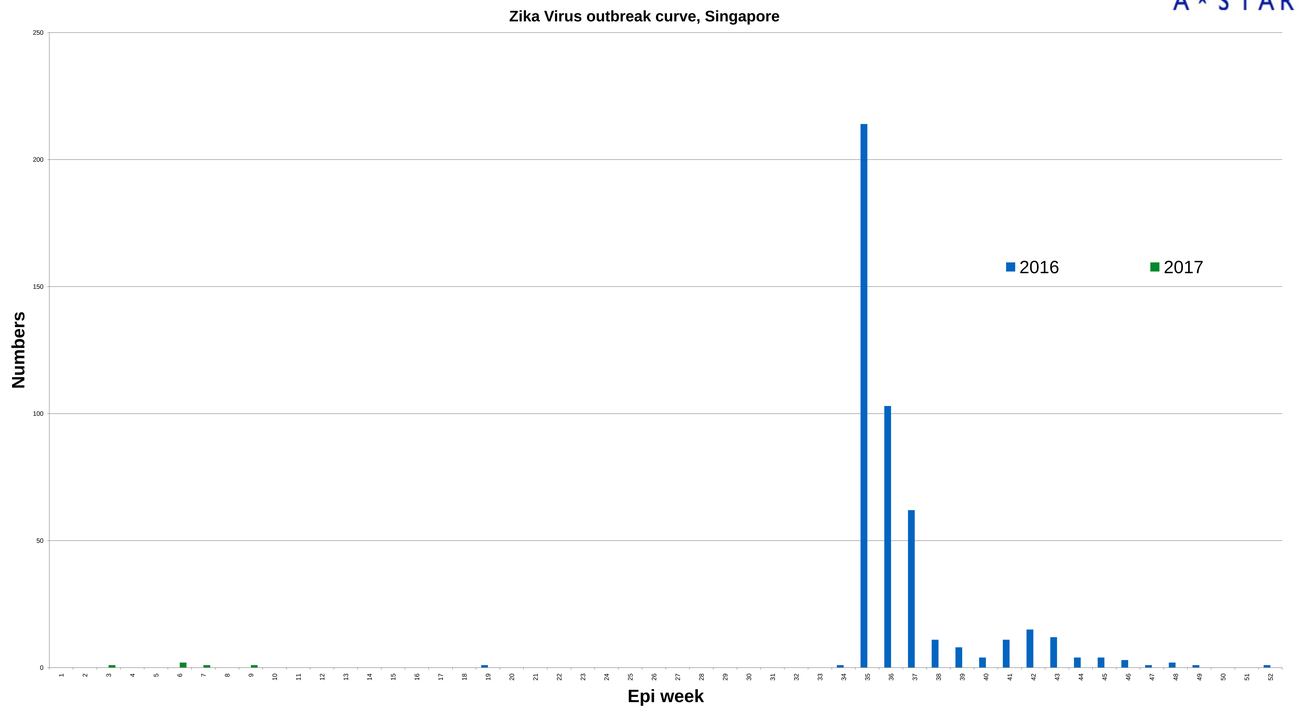
RESULTS

130 Zika positive cases with both Dengue NS1 results & ZikaV rt-PCR. Ct values varied from 22 to 39

127 /130 had a **negative** Dengue NS1 antigen
3 /130 had a **positive** Dengue NS1 antigen result
- ZikaV Rt-PCR ct values all weak at 38, 39 & 39
- possibly contamination events

Two of the three were Dengue rt-PCR positive
- one serotype 1 and one serotype 3

So the positive Den NS1 antigen was appropriate
So these 2 were not false positive NS1



DISCUSSION - 1

The 3RD case was:
- Dengue rt-PCR Negative
- Dengue IgM Negative
- Dengue IgG Positive.

The negative DenV rt-PCR does not contribute to the discussion as samples were collected too late, 12-15 days after onset of symptoms.

Repeated ZikV rt-PCR with two assays were both positive (ct = 38 and 33). He had had Zika!

The positive DenV IgG can't distinguish old and irrelevent dengue from recent 2^{o} dengue so a dual infection can't be confirmed or refuted.

The DenV IgG may also be a false positive, either due to cross reacting Zika antibodies or to laboratory error.

DISCUSSION – 2

Many cases with a strong ZikaV rt-PCR ct, some as low as 22, did not have a false positive DenV NS1 antigen test.
It seems unlikely that the 3rd case would have had a false positive DenV NS1 antigen test when the ZikaV rt-PCR ct was so weak, at 38.
This argument assumes the ct value reflects the amount of antigen in the circulation.

CONCLUSION

Only 1/130 patients with ZikaV might have had a false positive Dengue NS1 result, suggesting that any cross reaction is very unusual, if it occurs at all, with this NS1 assay

'No disclosures'