Can Zika virus antibodies cross-protect against dengue virus?

Guilherme Ribeiro and colleagues (February, 2018) report a major downward trend in dengue virus infection cases after the recent Zika virus outbreak in the Americas. They used epidemiological data collected between 2009 and 2017 in Salvador, Brazil, to suggest that the decline in dengue virus infection cases observed since 2015 could be the result of cross-protective immunity to dengue virus induced by Zika virus infection.

As part of the National Reference Centre for Arboviruses, we do neutralisation assays for a variety of arboviruses, including Zika and dengue viruses. Between 2016 and 2017, we examined 382 human serum samples (from 323 patients) for Zika virus neutralising antibodies. A subset of 55 serum samples (from 44 patients) were examined for in-vitro neutralising potential against both Zika virus and dengue virus serotypes 1-4. Samples with low Zika virus neutralisation titres (unlikely to be Zika) and high dengue virus neutralisation titres (likely to be dengue) were removed from the subset before further analysis. In a serum sample with pre-existing dengue virus neutralising antibodies, measuring the specific contribution of Zika virus antibodies to the neutralisation of dengue virus is difficult (if not impossible). Therefore, we limited our analysis to dengue virus-naïve patients with a documented Zika virus infection (confirmed by PCR or virus neutralisation; n=21) and investigated dengue virus neutralisation potential in vitro. Only one of 21 Zika virus serum samples showed a weak cross-neutralisation titre (the neutralisation titre that inhibited 90% of viral infection \(NT_{90}\) was 86) against dengue virus serotype 2, and two additional serum samples showed \(NT_{50}\)≥50. This finding is in line with earlier reports that showed the absence of Zika virus neutralisation among primary dengue virus infections and low-frequency cross-neutralisation in repeat dengue virus infections, suggesting that independent neutralising antibody populations against these two viruses are raised. This picture is more complex in a population with pre-existing flavivirus immunity resulting from previous exposures to flaviviruses other than Zika or vaccination, as is the case in Latin America, and the attribution of immunity against Zika virus to dengue infection in such a population can only be determined when pre-Zika infection archived serum samples are available. Of note, the epidemiological data presented by Ribeiro and colleagues already showed a downward trend in dengue virus infection cases in 2012 and 2013, before the Zika virus epidemic occurred. The further decline in dengue virus infections in 2016 and 2017 could merely result from existing immunity against dengue virus in the population of Salvador, and not necessarily from Zika virus antibodies that cross-protect against subsequent dengue virus infections.

We declare no competing interests. The National Reference Centre for Arboviruses is partially supported by the Belgian Ministry of Social Affairs through a fund within the Health Insurance System. The Institute of Tropical Medicine is a member of the ZikaPLAN consortium that received funding from the European Union’s Horizon 2020 research and innovation programme under ZikaPLAN (grant agreement 734584).

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