Zika virus diagnostics

Ana Bispo & David Brown, Flavivirus Laboratory, Instituto Oswaldo Cruz, Fiocruz, Rio de Janeiro.

Laboratory diagnosis of Zika virus (ZIKV) infection relies on virus isolation and nucleic acid, antigen and antibody detection. The virus can be detected in a wide range of biological samples, with low levels in blood only reliably detectible within 6 days of illness onset. Cell culture is time consuming and of limited sensitivity for diagnosis. Testing of urine samples is recommended for up to 14 days after onset.

When the first wave of ZIKV infection hit Brazil in 2015, no one was prepared and laboratories rapidly established in-house real-time RT-PCR assays. At present, most laboratories in Brazil are running in-house assays based on the published Lanciotti ZIKV real-time RT- PCR assay, with sensitivity to detect between 25 and 500 viral RNA copies. As negative results from these assays do not rule out infection, given the 6 day window of detection, reports that Zika virus RNA can be detected consistently for longer in whole blood (up to 2 months), saliva and urine (up to 3 months) and semen samples (up to 6 months) are promising.

WHO has developed an Emergency Use Assessment and Listing (EUAL) procedure to assess the safety, quality and performance of in vitro diagnostics to expedite their availability. Two assays with sensitivity in the range of 100 IU/ml (CI) have currently been assessed, AccuPower® ZIKV (DENV, CHIKV) Multiplex Real-Time RT-PCR Kit manufactured by Bioneer Corporation and RealStar® Zika Virus RT-PCR Kit 1.0 manufactured by Altona Diagnostics GmbH.

Serology based on ZIKV IgM detection is recommended >14 days from illness onset, as IgM develops in the first week of infection and persists up to 12 weeks. Results should be interpreted carefully in Latin America and other endemic areas, where high background exposure to other flaviviruses is likely and false positive results are caused by cross-reactivity with dengue virus antibodies. A proportion of ZIKV infections in the outbreak region will mount a secondary immune response with low IgM, further complicating interpretation. Currently, capture IgM assays using cultured virus antigen and indirect Zika NS1 IgM assays are available, but have neither high sensitivity nor specificity in the Brazilian population. Several IgM assays recently approved by the FDA approval must still be tested in Latin American populations. A range of new Zika IgG assays are in development using recombinant type specific proteins (NS1, ED3) and different formats, which also hold promise for more specific serological diagnosis.

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement No 734857