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Clinical management of pregnant women exposed to Zika virus

We read with interest the recent work about Zika virus in *The Lancet Infectious Diseases*[1,2] and *The Lancet*.[3] Even if still yet to be confirmed, the association between infection during pregnancy and birth defects is alarming. Recommendations for management of pregnant women at risk of Zika virus infection (ie, those living in endemic areas or who travelled to an area with active virus circulation), are urgently needed. In this Correspondence, we, as perinatal and infectious diseases specialists suggest a detailed management algorithm to help health-care providers (appendix). These recommendations should be adapted to local guidelines, as well as to any further updates on Zika virus.

Since 80% of patients infected with Zika virus are asymptomatic, we propose screening is offered to all pregnant women potentially exposed to the virus. The testing method should be carefully chosen according to the presence and timing of symptoms and done in reference centers. Unlike closely related infections (dengue, chikungunya), there is no abrupt onset of symptoms in Zika fever and determination of the timing of illness is challenging. Therefore, we recommend testing of multiple samples for Zika virus RNA and assaying of serum samples. In addition to blood, molecular detection of Zika virus in saliva can increase the detection rate of the virus in the acute phase of the disease, and urine can increase the window of detection.[4] Serological cross-reaction with other flavivirus is frequently observed, especially in secondary flavivirus infections (ie, past infections with another flavivirus), in both IgM detection and neutralisation tests. In endemic countries, laboratory screening might be difficult due to the number of suspected cases, and testing can exceed laboratories' capabilities.

Ultrasound monitoring of at-risk pregnancies is required independently of maternal Zika virus status and subsequent management needs to be based on the presence of ultrasound anomalies only. Amniocentesis should be done after 6 weeks from exposure and not before 21 weeks' gestation.[3] Correlation between head circumference in-utero and microcephaly at birth is more accurately measured in the third trimester, although it is still not optimal. Therefore, at least one ultrasound should be done after 28 weeks' gestation.

In asymptomatic newborn babies from mothers with confirmed Zika virus infection during pregnancy, latent anomalies should be carefully evaluated. Long-term complications of congenital infections with Zika virus are still not known, but as for congenital cytomegalovirus and toxoplasmosis infections, neurological development, eye fundus, and hearing should be assessed. In the presence of birth defects, an alternative diagnosis needs to be excluded, especially other congenital infections, genetic or syndromic anomalies, and perinatal injuries.[5]

We declare no competing interests.

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Published Online
April 4, 2016
http://dx.doi.org/10.1016/S1473-3099(16)30008-1

See Online for appendix

Zika virus associated deaths in Colombia

Zika virus infection has emerged in Latin America as an important threat due to its association with Guillain-Barré syndrome, which can lead to deaths, and microcephaly in newborn babies.[1–3] Cases of fatal Zika virus infection are rare and misunderstood. The spectrum of clinical disease remains uncertain and considering the rapidly evolving epidemics of this new arbovirus in Latin America, it deserves further detailed assessment.[1–4] Here,

Published Online
April 7, 2016
http://dx.doi.org/10.1016/S1473-3099(16)30006-8

For the **Rapid Risk Assessment** see http://ecdc.europa.eu/en/publications/Publications/zika-virus-rapid-risk-assessment-8-february-2016.pdf

we describe four well documented fatal cases of Zika virus infection in Tolima, Colombia.

Between Oct 2 and Oct 22, 2015, four febrile patients attended Tolima's Hospitals in the central region of Colombia. Patients were a 2-year-old girl, a 30-year-old woman, a 61-year-old man, and a 72-year-old woman, with 2–6 previous days with fever. The infant girl also had dehydration, somnolence, hepatomegaly, mucosa haemorrhage, and thrombocytopenia, evolving to respiratory distress, disseminated intravascular coagulation, and shock. The 30-year-old woman had exanthema in upper and lower limbs, severe thrombocytopenia, and leukopenia, evolving in 10 days to intracerebral and subarachnoid haemorrhages, sepsis, acute respiratory failure, seizures, and shock. The older man had myalgias and arthralgias, with dehydration, mucosa haemorrhage, also evolving to respiratory distress, acute coronary syndrome, and shock. This patient's history included high blood pressure under medication control. The older woman presented with abdominal pain, vomiting, dehydration, somnolence, and thrombocytopenia, evolving to acute respiratory failure and shock. This patient's history included diabetes mellitus type 2 under control with insulin. In all four patients, giving the endemicity of the zone, dengue fever or chikungunya were suspected. All patients presented with anaemia (haemoglobin range 90–120 g/L), three of them with leukopenia. The 30-year-old woman had leukocytosis, and all but the older man had severe thrombocytopenia (<14 000 platelets per mL). Despite medical management at the intensive care unit, all of four patients died. The infant girl died 24 h after admission (5 days after symptoms began); the 30-year-old woman died after 10 days (12 days after symptoms began); the 61-year-old man at 24 h (7 days after symptoms begun), and the 72-year-old woman in less than 24 h (48 h after symptoms began). In all these cases, RT-PCR for dengue (including tissues), anti-dengue IgM, and NS1 ELISA and western-blot tests were negative. In the 61-year-old man, IgM for chikungunya was positive. IgM for *Leptospira* spp was negative in all cases. Finally, in all patients RT-PCR for Zika virus was positive, confirmed at the Colombia national reference laboratory. In the infant girl and 30-year-old woman, necropsy revealed probable acute leukaemias (lymphoblastic and myeloid, respectively). In the 61 year-old man, necropsy showed ischaemic lesions in the brain with areas of necrosis in the liver and of systemic inflammatory response in the spleen. In this patient, RT-PCR of tissues was positive for Zika virus. In the 72-year-old woman, necropsy showed oedema and ischemic lesions in brain.

From Sept 22, 2015, to March 19, 2016, there were 58 838 cases of Zika virus infection in Colombia (2361 laboratory-confirmed, 49 211 diagnosed by clinical criteria, and 7266 suspected); nevertheless before the current report, only one previous fatal case has been described, from our group in Colombia.[4] Before the current outbreak in Latin America, Zika virus was not linked to deaths,[1,3,4] but as of Nov 28, 2015, the Brazil Ministry of Health has also reported three deaths associated with Zika virus infection (two in adults and one in a newborn baby).[5] These cases call attention to the need for evidence-based guidelines for clinical management of Zika, as well as the possible occurrence of atypical and severe cases (including possibly congenitally-related microcephaly).[2,3,5] Based in our first case report,[4] such guidelines have been considered and suggested by the European Centre for Disease Control in its recent Rapid Risk Assessment.

We declare no competing interests.

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Published **Online** April 7, 2016 http://dx.doi.org/10.1016/S1473-3099(16)30007-X

Epidemiological data accessibility in Brazil

Concerns about data sharing and transparency during epidemiological emergencies are not new.[1–4] Dye and colleagues[5] have announced an initiative called Zika Open through which the manuscripts and respective data submitted to *Bulletin of the World Health Organization* would be publlished as open access from the date of submission onwards, under a Creative Commons License (CC BY IGO 3.0). This is an important initiative. Here we report challenges faced, particularly in Brazil, for timely, lawful access to governmental collected disease-notification data that are essential to understand the current Zika virus epidemic, and any future public health emergency.

Brazil has a country-wide disease notification system, SINAN, that allows for continuous assessment of epidemiological dynamics throughout the country. Created in the 1990s, it continually records cases of many diseases via compulsory notification by health-care facilities all over the