The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

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Care of women with confirmed Zika virus infection during pregnancy in Australia

Early evidence for vertical transmission of Zika virus

In October 2015, an unusual increase in the birth incidence of microcephaly was reported in Brazil, spatio-temporally associated with a local epidemic of Zika virus infection (1). While the exact contribution of Zika virus infection to these increased reports of microcephaly is still unresolved (2), there are accumulating case reports of vertical transmission of Zika virus in association with serious perinatal morbidity and mortality. Microcephaly and central nervous system (CNS) abnormalities are specific clinical features that have been reported in fetuses and newborns with laboratory-confirmed infections. (3,4,5,6) However, the scientific data on the biological mechanisms of transmission are still scarce. There is currently no specific antiviral therapy for maternal Zika virus infection, either to prevent or treat perinatal transmission. Due to the considerable concern regarding the risk of fetal abnormalities following infection during pregnancy, the following recommendations are provided for maternity health providers in Australia and New Zealand caring for women with confirmed Zika virus infections.

Referral for specialist opinion

Woman with (i) a history of travel during pregnancy to an area with ongoing Zika virus infection; AND (ii) positive serological or virological evidence of Zika virus infection (positive blood or urine PCR, or positive Zika virus serology) should be referred to a suitably qualified expert in diagnosis and management of perinatal infections (eg maternal fetal medicine specialist).

Women with a prenatal or postnatal diagnosis of fetal/newborn microcephaly or CNS abnormality should have a travel history taken to assess possible risk of Zika virus infection, in addition to the usual investigations for congenital CNS abnormalities (such as testing for syphilis, toxoplasmosis, rubella, cytomegalovirus, herpes virus infection, and chromosomal abnormalities).

Management of pregnant women with confirmed Zika virus infection

Ultrasound

A baseline ultrasound for fetal morphology and biometry should be performed for women with serological/virological evidence of Zika virus infection during pregnancy. (7,8).

If this examination is normal, serial ultrasounds at least every 4 weeks for fetal biometry and intracranial anatomy is recommended. Abnormalities associated with confirmed fetal/ newborn Zika virus infection that may be detected on prenatal imaging include (3,4):

Microcephaly

Intracranial calcifications

Corpus callosal and vermian dysgenesis

Cerebral ventriculomegaly

Eye abnormalities (cataracts, orbital asymmetry, intraocular calcifications)

Thalami and brainstem abnormalities

Severe arthrogryposis

Varied diagnostic cut-offs for microcephaly are in common use, with HC > 3 SD below the mean being one of the most specific definitions (1,9). In an otherwise normal neurosonogram, conclusions regarding the impact of Zika virus infection in fetuses with HC > 2 SD but < 3 SD below the mean should be made with caution.

Ultrasound remains the mainstay of diagnosis of microcephaly and intracranial pathology, but magnetic resonance imaging (MRI) may be considered as a complementary imaging modality after consultation with a team with appropriate expertise in fetal MRI. Any form of fetal imaging should only be offered in a setting with appropriate skills for interpretation.

Amniocentesis for Zika virus PCR

The role of amniocentesis in a woman with evidence of Zika virus infection but a morphologically **normal** fetus is uncertain as the rate of *in utero* infection, time course of transplacental viral passage, and the subsequent risk of fetal sequelae are unknown. In other congenital infections such as toxoplasmosis and cytomegalovirus, a minimum interval of 4-7 weeks from maternal infection, and a minimum gestational age of 18-21 weeks, are commonly observed criteria prior to performing amniocentesis (10,11). Comparable data for prenatal testing for Zika virus is unavailable. It is possible that amniocentesis may have a reduced sensitivity and hence poorer negative predictive value for congenital infection if performed too soon after maternal infection, particularly in the presence of normal ultrasound findings. Conversely, the risk of subsequent microcephaly and other fetal CNS complications following a positive amniocentesis result in the presence of a normal ultrasound is also unknown.

If fetal ultrasound examination is **abnormal** (microcephaly +/- CNS abnormalities), amniocentesis for Zika virus PCR should be considered, along with testing for other possible causes. The sensitivity and specificity of Zika virus PCR on amniotic fluid is currently unknown, but is assumed to be similar to serum. Positive prenatal diagnoses on amniotic fluid have only been reported in fetuses with severe CNS abnormalities in the third trimester (3). There has been one report from Brazil on the presence of Zika virus in the placenta of a women who had a first trimester miscarriage (9).

Microcephaly due to congenital Zika virus infection may be an evolving condition, and so may only become apparent in the late second or third trimester. Given the potentially serious neurological disability, patients may seek termination of pregnancy and clinicians should be aware of their local jurisdictional limitations around access to late termination of pregnancy.

Peripartum transmission

Not all perinatal transmission results in severely affected fetuses/newborns. A report of peripartum transmission in two mildly affected term newborns in French Polynesia was published in 2014. (12) In these cases, the clinical symptoms in the mothers occurred within two weeks of birth. The maternal sera were PCR positive within two days of delivery and in their newborns within the first four days of life. In these women, Zika viral particles were also detectable in breast milk, but no replicative particles were present on viral culture. The timing of infection (in utero, intrapartum or postpartum) was unable to be definitively determined in either case. Infection through oral intake is not known and any effects of neonatal infection through breast feeding are thought to be mild. In line with other professional societies, RANZCOG does not consider breastfeeding to be contraindicated after maternal Zika virus infection (13).

Newborns with suspected congenital Zika virus should have their head circumference measured at birth and repeated 24 hours later. Newborn urine or saliva samples should be sent for PCR, and cord blood or newborn serology performed. The placenta should be sent for histological examination and Zika virus testing (eg. PCR, immunohistochemistry). If evidence of Zika virus infection is confirmed, the ophthalmic examination (including retinal examination), cranial ultrasound, and hearing screening should be performed. Ongoing follow-up for long term sequelae should be arranged. (14)

Notifications

Clinicians are reminded that Zika virus is a notifiable communicable disease in Australian and New Zealand and confirmed infections should be reported according to local requirements. Notification of birth defects deemed to be caused by congenital Zika virus infection should also be made to the relevant congenital anomaly registry.

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