Evaluation of Pregnant Women, Fetuses and Infants with Zika Virus Exposure and Infection: Lessons Learned from the Congenital Zika Program at Children’s National

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Abstract

Background: Zika Virus (ZIKV) infection during pregnancy has severe potential consequence to the fetus. Despite limited endemic transmission in the continental US, travel/sexual exposure in the preconception/pregnancy period requires experienced multidisciplinary care to assess potential infection and effects in the fetus.

Methods: The Congenital Zika Program at Children’s National (CZPCN) was developed to meet need for pre- and post-natal consultation and care. The CZPCN includes multidisciplinary expertise in fetal imaging, pediatric infectious diseases, fetal and pediatric neurology. Services include a hotline, facilitation of ZIKV testing and interpretation, detailed fetal MRI/US, delivery instructions to facilitate postnatal evaluation of ZIKV exposure/infected fetuses and educational outreach to providers regarding ZIKV.

Results: Since inception of the program, 90 maternal/infant dyads have been evaluated by the CZPCN. Data are reported for the first 50 dyads evaluated during the period Jan 2016-May 2017. 36 women/fetuses were referred for possible ZIKV infection during pregnancy (32 US residents who traveled, 2 with partner who traveled, 2 emigrants). An additional 14 women/infant pairs were evaluated following postnatal referral to our program. Exposure route included direct arboviral (89%) and/or potential sexual exposure (48%). Symptoms occurred in only 6/50 (12%). Exposure occurred in the peri-conception period in 10/50 (20%), first trimester in 23/50 (46%), second trimester in 13/50 (26%), and third trimester 4/50 (8%). Nearly 50% (24/50) of women presented outside the 12 week window following exposure and could not have infection excluded. ZIKV was confirmed in 22% (11/50) or suspected due to unspecified flavivirus infection in 28% (14/50). Only 7/50 (14%) had negative PCR/IgM testing in appropriate window to exclude infection. Two fetuses with severe involvement were not carried to term, 1 was carried to term but died immediately after birth and 1 died within the first year of life.

Conclusion: CZPCN fills a critical need within our region to facilitate evaluation of exposed/infected pregnant women/fetuses/infants including multidisciplinary follow-up of affected surviving infants. Lessons learned are instructive to other centers developing Zika programs, which are needed as the range of endemic Zika transmission expands.

Background: Zika Virus (ZIKV) infection during pregnancy has severe potential consequence to the fetus. There has been limited endemic transmission of Zika virus in the continental US (Florida and Texas) however, US residents and their sexual contacts frequently travel to areas of endemic transmission.

As of September 13, 2017

- Continental US: 5,517 symptomatic ZIKV cases
- 2,679 pregnant women with lab evidence
- US Territories: 37,062 symptomatic ZIKV cases
- 4,055 pregnant women with lab evidence
- Arboviral or sexual exposure to Zika virus in the preconception/pregnancy period requires experienced multidisciplinary care to assess potential infection and effects in the fetus and newborn

Methods

- Referral Guidelines and Hotline for providers and patients
- Prenatal Consultation: Pregnant mother/fetus
- Postnatal Consultation: Newborns and Infants
- Single visit multidisciplinary evaluation
- Counseling and up-to-date guidance regarding ZIKV exposure and infection
- Coordination of testing with all state health departments
- Interpretation of testing
- Coordination of multidisciplinary evaluations for exposed/infected infants
- Audiology ad Ophthalmology Assessments
- Neurodevelopmental Follow-up
- Coordination with delivery hospital, obstetricians, MFM’s, pediatricians for subsequent monitoring

Advanced Fetal Imaging

- Fetal ultrasound ( Screening)
- Fetal MRI (Neuroradiologic technique)
- Detection of more subtle/earlier evidence of impaired fetal brain growth/development

Advocacy

- Professional education:
  - >20 community Grand Round lectures in Greater Washington DC area
- Direct outreach to OB and MFM practices in region
- Member of CDC Zika Care Connect
- Network of specialized providers
- Expert panels for US Senate and Congressional staff briefings/roundtables on Zika
- Education with AAP/CDC to other centers developing Zika programs
- Chair/Convene State of Art sessions at PAPS and ID Week

Research:

- Clinical and Basic Science Research in US and Colombia
- Fetal Imaging –serial fetal MRI and ultrasound
- Viral isolates- Quantitative PCR, serologic
- Genetics: Maternal/Fetal
- Long term neurodevelopmental follow-up of infants
- Neuropsychological characterization of fetal brain

Results

- Between Jan 2016 and May 2017:
  - 50 maternal/infant dyads evaluated
  - 36 women/infants referred for possible ZIKV infection during pregnancy
    - 32 with direct travel-related exposure
    - 2 without travel; sexual exposure/partner traveled
    - 2 recent emigrants from endemic areas
  - Additional 14 postnatally referred women/infant pairs due to:
    - Maternal prenatal exposure
    - Microcephaly/Ventriculomegaly
    - Microphalma
    - Arthrogryposis
- Exposure Summary
  - Route: Direct arboviral (89%)
  - Additional potential sexual exposure (48%)
  - Timing of Exposure/Infection:
    - 20% (10/50) in Peri-conception period
    - 46% (23/50) in First Trimester
    - 26% (13/50) in Second Trimester
    - 8% (4/50) in Third Trimester
- Symptoms:
  - Only 12% (6/50) of women symptomatic
  - 88% (45/50) asymptomatic
  - Fetal CNS abnormalities detected in BOTH groups
- ZIKV Testing:
  - 48% (24/50) presented outside of appropriate window for sensitive PCR or IgM detection
  - 22% (11/50) with confirmed ZIKV infection
  - 28% (14/50) with confirmed Flavivirus infection unspecified
  - Only 14% (7/50) with negative PCR and/or IgM testing in appropriate window to exclude infection
  - 36% (18/50) could not have infection excluded

Outcomes:

- 8/ (450) fetuses/infants with severe CNS involvement
  - all detected by prenatal evaluation/imaging
- 2 not carried to term
- 1 carried to term but died immediately after birth
- 1 died within the first year of life

Conclusions

- The Congenital Zika Program at Children’s National fills a critical need within the Washington DC metropolitan region to facilitate referral and evaluation of ZIKV exposed/infected pregnant women/fetuses/infants
- 90 maternal/infant dyads evaluated since inception of program in January 2016
- The majority of ZIKV-exposed women do not have clear-cut testing results due to limitations of timing between exposure and evaluation, or limitations of testing specificity/flavivirus cross-reactivity
- Counseling of pregnant exposed/infected women is complex, time-sensitive, and stressful and requires multidisciplinary expertise
- Fetal MRI may provide earlier evidence of ZIKV-induced fetal brain injury compared to fetal US
- Large prospective study in Colombian research cohort ongoing
- Post-natal evaluation and follow-up of infants in whom infection cannot be excluded (not only proven infected infants) is critical and requires central coordination
- Lessons learned are instructive to other centers developing Zika programs, which are needed as the range of endemic Zika transmission expands