Middle cerebral artery Dopplers and adverse neonatal outcomes among pregnant women with Zika virus infection

1Thalia Wong MD, 2Jose Paulo Pereira Jr MD PhD, 3Nasim Sobhani MD,
2Renan Fonseca Cardozo MD, 2Helena Abreu Valle MD, 2Beatriz Ribeiro Torres
Dutra MD, 2Helder Dotta Gama MD, 3Stephanie L. Gaw MD PhD

1. Division of Maternal Fetal Medicine, University of California, Los Angeles
2. Instituto Fernandez Figueira/Fiocruz, Rio de Janeiro, Brazil
3. Division of Maternal Fetal Medicine, University of California, San Francisco
Background

• Zika virus (ZIKV) infection in pregnancy causes a spectrum of adverse perinatal outcomes
  • Fetal demise
  • Fetal growth restriction
  • Abnormalities of the central nervous system
• Evidence for methods of prenatal surveillance of ZIKV infected pregnancies is limited
Objective

To investigate the role of MCA Doppler measurements for the prediction of abnormal neonatal outcomes in pregnancies affected by Zika virus
Study Design

• Secondary analysis of a prospective cohort study
  • Women diagnosed with ZIKV during pregnancy
  • September 2015 to December 2016
  • Single regional referral center in Rio de Janeiro, Brazil
• Each patient underwent prenatal ultrasonography and **MCA values** were collected
  1. **Peak systolic velocity** (PSV)
  2. PSV **multiple of the median** (MoM) calculated for gestational age
  3. **Pulsatility index** (PI)
• Perinatal data collect at time of birth and each neonate underwent complete physical exam
Study Design

• **Primary outcome was a composite adverse neonatal outcome**
  • Perinatal death
  • Abnormal neonatal outcome:
    • Physical exam
    • Fundoscopy exam
    • Hearing exam
  • Abnormal postnatal neuroimaging
    • Ultrasound
    • CT
    • MRI
Statistical Analysis

• MCA Doppler values of normal and abnormal neonatal outcomes were compared with **Wilcoxon rank sum test**
  • Analytic weight incorporated to account for multiple ultrasound measurements

• Predictive value of MCA Dopplers for the development of abnormal neonatal outcome in ZIKV-affected pregnancies was calculated by **logistic regression**
145 pregnant women PCR-positive for ZIKV + at least one prenatal ultrasound (September 2015 – December 2016)

Inclusion criteria:
- MCA Doppler measurements performed
- Known neonatal outcomes

127 pregnant women

Serial ultrasounds performed (Range: 1-8)

MCA Doppler values collected

MCA PSV
n = 314

MCA PSV MoM
n = 314

MCA PI
n = 359

Normal Neonatal Outcome
n = 57

Abnormal Neonatal Outcome
n = 70
Pregnancy Characteristics

• Median maternal age = 29 years (IQR 24-33)
  • 24 (18.9%) advanced maternal age (> 35 years)

• Trimester of infection

  • Over half the patients developed infection in the 2nd trimester

<table>
<thead>
<tr>
<th>Trimester</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trimester</td>
<td>40</td>
<td>31.5%</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>70</td>
<td>55.1%</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>6</td>
<td>4.7%</td>
</tr>
<tr>
<td>Unknown</td>
<td>11</td>
<td>8.7%</td>
</tr>
</tbody>
</table>
Pregnancy Outcomes

Mode of Delivery

- Median gestational age at delivery
  38 weeks 4 days (IQR 37.75 – 39.47)
- Median birthweight
  3145 grams (IQR 37.75 – 39.47)
- 44 NICU admissions – median length of stay
  9 days (IQR 5 – 16)
Adverse neonatal outcomes

70 infants with composite adverse neonatal outcome

- Abnormal postnatal imaging (n = 41)
  - Ultrasound - 28
  - CT - 24
  - MRI - 19

- Abnormal postnatal exam (n = 59)
  - Clinical Exam - 55
  - Fundoscopy Exam - 18
  - Hearing Exam - 7
Middle cerebral artery Doppler values in ZIKV-infected pregnancies

<table>
<thead>
<tr>
<th></th>
<th>Normal Neonatal Outcome (n = 57)</th>
<th>Abnormal Neonatal Outcome (n = 70)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCA PSV (cm/sec)</strong></td>
<td>46.5 (34.0 – 58.0)</td>
<td>42.0 (27.0 – 53.0)</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>MCA MoM</strong></td>
<td>1.04 (0.92 – 1.21)</td>
<td>0.98 (0.71 – 1.12)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>MCA PI</strong></td>
<td>1.87 (1.65 – 2.14)</td>
<td>1.88 (1.57 – 2.11)</td>
<td>0.998</td>
</tr>
</tbody>
</table>

- Lower MCA PSV values and MoM associated with abnormal neonatal outcomes
- No significant difference in neonatal outcomes based on MCA PI
Middle cerebral artery Doppler values in ZIKV-infected pregnancies

Gestational Age at Ultrasound (weeks)

- MCA PSV (cm/sec)

Normal Neonatal Outcome

Abnormal Neonatal Outcome
Lower MCA PSV measurements associated with abnormal neonatal outcomes

Each 1 cm/sec decrease in MCA PSV associated with a 6.2% increased probability of abnormal neonatal outcome

MCA PSV of 30 cm/sec with a 75% predicted probability of an abnormal neonatal outcome
(95% CI: 62%-88%)
Conclusion

• Lower MCA PSV measurements are associated with abnormal neonatal outcomes in Zika Virus infected pregnancies

• Evaluation of MCA Dopplers may be of clinical utility in the surveillance of ZIKV-affected pregnancies
Questions?

E-mail Dr. Wong at thaliawong@mednet.ucla.edu