Does delivery after 40 weeks gestation increase maternal to child transmission of HIV in well controlled HIV positive pregnancies?

The preliminary results of a secondary analysis of the NISDI/LILAC cohort

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Management of Delivery in HIV Positive Pregnancies

- Standard of care to deliver via cesarean delivery (CD) for poorly-controlled HIV at 38 weeks estimated gestational age (EGA)
- Standard of care to deliver well-controlled HIV positive pregnancies at or before 40 weeks EGA
Risks of Induction of Labor

- Prolonged labor
- Failed induction
- Cesarean delivery

- Higher rates of complications in HIV positive women
  - Infection
  - Surgical trauma
  - Extended hospitalizations
  - Death
Management of Delivery in HIV Uninfected Pregnancies

- Expectant management until induction for late term 41 weeks EGA
  - Lower rates of perinatal death
  - Lower rates of infant morbidity
  - Lower rates of cesarean section
Hypotheses and approach

1. We hypothesized that there would be no increase in MTCT associated with delivery on or after 40 weeks EGA in well controlled HIV positive pregnancies
   - Examine incidence of MTCT in deliveries between 40 and 41 weeks EGA compared to control deliveries between 38 weeks and 39 weeks and 6 days EGA

1. We hypothesized that there would be no increased maternal or neonatal morbidity or mortality associated with delivery on or after 40 weeks EGA in well controlled HIV positive pregnancies
   - Compare maternal pregnancy outcomes
   - Compare neonatal outcomes
Methods: Study Design

- Secondary analysis of NICHD International Site Development Initiative (NISDI) Perinatal/Longitudinal Study in Latin American Countries (LILAC)
- Matched cohorts of HIV positive pregnancies <40 weeks EGA compared to ≥40 weeks
Definitions:

- Well controlled HIV: Viral load (VL) less than 1000
- Pregnancies <40 weeks EGA: 38w0d-39w6d
- Pregnancies ≥40 weeks EGA: 40w0d-41w0d
- Gestational age determined by:
  - Capurro
  - Obstetrical estimate
  - Pediatric newborn exam (Ballard)
Methods: Statistical Analysis

- Associations between EGA and outcomes were examined through bivariate analyses, with Fisher’s exact or Wilcoxon nonparametric p-values.
- We plan to use mixed model methods for continuous outcome measures and bivariate conditional logistic regressions for categorical outcome measures.
- We plan to use multivariate conditional logistic regression and mixed models that can control for the correlations among the matched observations for our modeling analyses.
Results: Study population

- Women enrolled in NISDI Perinatal/LILAC protocols, N=1630
  - HIV RNA VL <1000 at time of delivery, N=1242
    - Singleton birth, N=1226
      - Live birth, N=1213
        - Term birth (≥38 weeks), N=927
          - EGA < 40 weeks, N=620
          - EGA ≥40 weeks, N=307
            - Infant HIV status unknown (missing), N=12
              - Infant has known HIV status (final analysis population), N=915
            - Preterm birth (< 38 weeks), N=285
              - Stillbirth, N=11
              - Spontaneous abortion, N=2
        - Preterm birth (≥38 weeks), N=1
  - Multiple births, N=16
  - HIV RNA VL ≥ 1000 at time of delivery, N=249
  - HIV RNA VL missing at time of delivery, N=139
## Results: Maternal Demographics

<table>
<thead>
<tr>
<th></th>
<th>&lt;40 weeks EGA N= 612</th>
<th>≥40 weeks EGA N= 303</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age in Years</td>
<td>28.1</td>
<td>28.6</td>
<td>0.32</td>
</tr>
<tr>
<td>HIV VL</td>
<td>156.9</td>
<td>141.2</td>
<td>0.15</td>
</tr>
</tbody>
</table>
Results

Maternal to Child Transmission
## Results: Neonatal HIV Status

<table>
<thead>
<tr>
<th></th>
<th>Pregnancies &lt;40 weeks EGA N = 612</th>
<th>Pregnancies ≥40 weeks EGA N= 303</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indeterminate:</td>
<td>32 (5.2%)</td>
<td>14 (4.6%)</td>
</tr>
<tr>
<td>Presumed uninfected:</td>
<td>3 (0.5)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Uninfected:</td>
<td>573 (93.6%)</td>
<td>286 (94.4%)</td>
</tr>
<tr>
<td>HIV-infected:</td>
<td>4 (0.7%)</td>
<td>2 (0.7%)</td>
</tr>
</tbody>
</table>

p=1.00
Results:

Maternal Pregnancy Outcomes
### Results: Mode of Delivery

<table>
<thead>
<tr>
<th></th>
<th>&gt;40 weeks EGA N= 612</th>
<th>&lt;40 weeks EGA N= 303</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal Delivery</td>
<td>224 (36.6)</td>
<td>176 (58.1)</td>
</tr>
<tr>
<td>Elective CD</td>
<td>276 (45.1)</td>
<td>76 (25.1)</td>
</tr>
<tr>
<td>Non-elective CD</td>
<td>111 (18.1)</td>
<td>51 (16.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 ( 0.2)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

p <.0001
# Results: Indication for Cesarean Delivery

<table>
<thead>
<tr>
<th>Indication</th>
<th>&lt;40 weeks N=387 N (%)</th>
<th>≥40 weeks N=127 N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of HIV Infection</td>
<td>158 (40.8)</td>
<td>52 (40.9)</td>
</tr>
<tr>
<td>Repeat Cesarean Section</td>
<td>95 (24.5)</td>
<td>19 (15.0)</td>
</tr>
<tr>
<td>Non-Reassuring Fetal Heart Rate</td>
<td>15 ( 3.9)</td>
<td>12 ( 9.4)</td>
</tr>
<tr>
<td>Prolonged Rupture Of Membranes</td>
<td>17 ( 4.4)</td>
<td>9 ( 7.1)</td>
</tr>
<tr>
<td>Patient Desires Sterilization</td>
<td>17 ( 4.4)</td>
<td>0 ( 0.0)</td>
</tr>
<tr>
<td>Failed Induction**</td>
<td>13 ( 3.4)</td>
<td>8 ( 6.3)</td>
</tr>
<tr>
<td>Patient Request</td>
<td>20 ( 5.2)</td>
<td>2 ( 1.6)</td>
</tr>
<tr>
<td>Cephalopelvic Disproportion</td>
<td>17 (4.4)</td>
<td>6 (4.7)</td>
</tr>
<tr>
<td>Malpresentation</td>
<td>8 ( 2.1)</td>
<td>4 ( 3.1)</td>
</tr>
<tr>
<td>Active Or Recent Genital Infection</td>
<td>6 ( 1.6)</td>
<td>4 ( 3.1)</td>
</tr>
</tbody>
</table>

**p=0.1929
Results: Other Maternal Outcomes

- No difference in length of stay
- No maternal deaths
- Post-partum and post-operative complications too rare to draw any conclusions at this time
Results:

Neonatal Outcomes
Results: Neonatal Outcomes

• Higher proportion of neonates born <40 weeks EGA were low birth weight (LBW) (8.2%) compared to ≥40 weeks EGA (4.0%, p= 0.0173)

• Other neonatal complications too rare to draw any conclusions at this time
Summary

• Risk of MTCT did not differ by EGA
  – Not powered to demonstrate rates were equivalent
  – Challenges current standard of care

• We will complete multivariate logistic regression to better understand the increased LBW and indications for elevated CD in pregnancies which delivered <40 weeks EGA

• No difference in other maternal and neonatal outcomes
  – Not powered to demonstrate rates were equivalent
Limitations and Next Steps

• Underpowered to draw any conclusions regarding differences MTCT in pregnancies <40 weeks vs. ≥40 weeks EGA

• We are currently working to incorporate the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1025 data into the analysis for our primary and secondary outcomes of interest
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7. Gülmezoglu AM et al. Induction of labour for improving birth outcomes for women at or beyond term (Review); Cochrane Collaboration 2012; (4)