Background

- Preterm birth (PTB) is the leading cause of childhood morbidity and mortality
- PTB rates are higher in HIV-infected populations including those on ART
- Stillbirth, only a subset of births result in PTB
- Suggesting risk factors other than HIV infection are also important
- Role of inflammation in PTB needs further study in the setting of HIV
- Immune pathways involved are not clear
- Non-invasive immune markers with predictive value are lacking
- Objective of this study was to determine the association of select markers of inflammation in HIV-infected pregnant women

Methods

Population

- Sampled from Sputum Specimen Collection and Evaluation in Pregnancy (SWEN) trial between 2002-2007
- HIV-infected women started intrapartum nevirapine
- Newborns were randomized to receive one of two interventions:
  - Single dose of nevirapine
  - Extended dose through six weeks after birth
- Enrolled in sites from India, Ethiopia and Uganda

Study Design

- Nested Case-control Study
  - Total N=107; 26 cases and 81 controls
  - Only samples from India
  - Outcome: PTB (<37 weeks gestational age (GA))
  - Exposure: Inflammatory markers collected before labor (21-33 weeks GA)

- 4 biomarkers of inflammation measured using ELISAs:
  - FABP: marker of intestinal barrier dysfunction
  - sCD14 and sCD163: marker of monocyte activation/microbial translocation
  - CRP: acute phase response protein

Analysis

- Differences in covariates by cases or control status assessed by:
  - Fisher’s exact test for categorical variables
  - Wilcoxon rank-sum test for continuous variables
- Odds of PTB per log, increase of each inflammation marker was determined using univariable and multivariable logistic regression

Results

- Odds of PTB with increased levels of Inflammation markers
- Multivariable model

Table 2. Levels of inflammation markers among cases and controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n=107)</th>
<th>Cases (n=26) (%)</th>
<th>Controls (n=81) (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/L)</td>
<td>2.43 (1.73-3.26)</td>
<td>4.20 (3.35-5.25)</td>
<td>1.50 (1.24-1.87)</td>
<td>0.04</td>
</tr>
<tr>
<td>Log(CRP)</td>
<td>2.40 (1.73-3.26)</td>
<td>4.20 (3.35-5.25)</td>
<td>1.50 (1.24-1.87)</td>
<td>0.04</td>
</tr>
<tr>
<td>Log(CGHD)</td>
<td>20.67 (20.20)</td>
<td>20.56</td>
<td>20.61</td>
<td>0.49</td>
</tr>
<tr>
<td>Log(CGHD)3</td>
<td>20.67 (20.20)</td>
<td>20.56</td>
<td>20.61</td>
<td>0.49</td>
</tr>
<tr>
<td>Log(SCD14)</td>
<td>9.33 (9.10-10.00)</td>
<td>9.65 (9.65-10.00)</td>
<td>9.73 (9.65-10.00)</td>
<td>0.03</td>
</tr>
<tr>
<td>Log(SFABP)</td>
<td>19.43</td>
<td>19.43</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Log(SFABP)</td>
<td>19.43</td>
<td>19.43</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Association of pregnancy inflammation markers with PTB

<table>
<thead>
<tr>
<th>Univariable Model</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>0.86 (0.63-1.17)</td>
<td>0.32</td>
</tr>
<tr>
<td>Log(CRP)</td>
<td>1.30 (1.01-1.69)</td>
<td>0.04</td>
</tr>
<tr>
<td>Log(CGHD)3</td>
<td>1.30 (1.01-1.69)</td>
<td>0.04</td>
</tr>
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</tr>
</tbody>
</table>

Multivariable model adjusted to maximal age, BMI, education, parity, history of previous PTB, inverness, CD4+ T-cell count and viral load (at time of inflammation assessment), and maternal HIV treatment during pregnancy.

Conclusions

- In our analyses, there was an increased odds of PTB with increased levels of Inflammation markers
- Multivariable model adjusted to maximal age, BMI, education, parity, history of previous PTB, inverness, CD4+ T-cell count and viral load (at time of inflammation assessment), and maternal HIV treatment during pregnancy.

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