Challenges of discrepant HIV tests in pregnant women in the PrEP era – to treat or not to treat?

Anjuli D Wagner1, John Kinuthia2, Julia Dettinger1, Nancy Mwongeli1, Laurén Gómez1, Salpine Watoyi2, Alison L Drake1,3, Felix Abuna2, Jillian Pintye1, Ben Ochieng2, Daniel Odinga2, Grace John-Stewart1,3,4, Jared M Baeten1,3,4

1 Department of Global Health, University of Washington; 2 Research and Programs, Kenyatta National Hospital, Kenya; 3 Department of Epidemiology, University of Washington; 4 Department of Medicine, University of Washington; 5 Department of Pediatrics, University of Washington

Background

- Risk of HIV acquisition is high during peripartum period
- Risk of mother-to-child HIV transmission elevated during incident infection
- PrEP recommended during pregnancy in high burden settings as female-controlled HIV prevention option
- HIV retesting – HIV testing after a prior HIV negative test – is a cornerstone in antenatal and PrEP programs
- Discrepant results (i.e. one positive, one negative) can occur, reflecting either true or false positivity (Figure 1)
- Guidelines lacking for treatment decisions after discrepant rapid results in context of pregnancy and PrEP

Methods

- PrEP Implementation for Mothers in Antenatal Care (PrIMA) study (NCT03070600) cluster RCT of approaches for integrating PrEP into antenatal care in western Kenya
- Trial ongoing; included data January-November 2018
- HIV-negative pregnant women tested monthly during pregnancy, at 6 & 14 weeks, 6 & 9 months postpartum
- Kenyan national algorithm used for testing (Figure 1); discrepant results tested by DNA PCR
- Women with discrepant results advised to initiate ART while awaiting PCR results

Results

- Among 3,031 women, 6,182 HIV retest sessions conducted, 8 discrepant rapid results (0.13%, 95% CI: 0.06-0.25%) among 6 women
- 5 women not using PrEP at time of testing; 1 initiated PrEP, but reported poor adherence and had not taken PrEP within 14 days prior to HIV test
  - Median time to PCR results 21.5 days (range 14-37)
  - All PCR negative, confirming HIV negative status (Table 1)
- While awaiting PCR results, none of the women initiated ART
- At later visits, 2 women had recurrent discrepant rapid results with negative PCRs when retested; one had concordant positive rapid results at delivery; she initiated ART and had two negative PCRs and negative ELISA

Pros and cons of immediate treatment of women with discrepant results while awaiting PCR

<table>
<thead>
<tr>
<th>First test</th>
<th>Second test</th>
<th>Third test</th>
<th>Fourth test</th>
<th>Fifth test</th>
<th>Days to PCR results</th>
<th>PrEP user</th>
<th>Weeks pregnant at postpartum</th>
<th>Initiated ART</th>
<th>Final HIV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>R (D)</td>
<td>NR (FR)</td>
<td>R (D)</td>
<td>NR (FR)</td>
<td>Negative DNA PCR (FP)</td>
<td>28</td>
<td>No</td>
<td>20 wk pregnant</td>
<td>Yes</td>
<td>Negative*</td>
</tr>
<tr>
<td>R (D)</td>
<td>NR (FR)</td>
<td>R (D)</td>
<td>NR (FR)</td>
<td>Negative DNA PCR (FP)</td>
<td>37</td>
<td>No</td>
<td>38 wk pregnant</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>R (D)</td>
<td>NR (FR)</td>
<td>R (D)</td>
<td>NR (FR)</td>
<td>Negative DNA PCR (FP)</td>
<td>21</td>
<td>No</td>
<td>37 wk pregnant</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>R (D)</td>
<td>NR (FR)</td>
<td>R (D)</td>
<td>NR (FR)</td>
<td>Negative DNA PCR (FP)</td>
<td>22</td>
<td>No</td>
<td>26 wk pregnant</td>
<td>No</td>
<td>Negative**</td>
</tr>
<tr>
<td>R (D)</td>
<td>NR (FR)</td>
<td>R (D)</td>
<td>NR (FR)</td>
<td>Negative DNA PCR (FP)</td>
<td>14</td>
<td>Yes</td>
<td>34 wk pregnant</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>NR (D)</td>
<td>R (HIV &amp; Syphilis dual test)</td>
<td>NR (FR)</td>
<td>Negative DNA PCR (FP)</td>
<td>16</td>
<td>No</td>
<td>26 wk pregnant</td>
<td>No</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

R: Reactive; NR: Non-reactive; (D) Determine; (FR) First Response; (FP) Filter paper
- Recurrent discrepant at next visit (36 weeks pregnant) but PCR negative; concordant rapid positive at delivery, PCR negative, follow up PCR and ELISA negative
- Recurrent discrepant at next visit (30 weeks pregnant), no PCR taken

** Recurrent discrepant at next visit (30 weeks pregnant), no PCR taken

Discrepant rapid results in context of pregnancy and PrEP

- CLINICALLY, false positive results occur during pregnancy due to cross-reactivity with autoantibodies & alloantibodies
- Clinical, emotional, interpersonal, logistical reasons in favor and against treatment while awaiting PCR results (Figure 2)
- Point-of-care viral testing may be helpful, tailored strategy to confirm diagnosis in such limited cases
- Need for guidelines to clarify public health approaches for programs providing PrEP in pregnancy

Conclusions

- As true HIV incidence decreases with PrEP and retesting, discrepant results will be observed in program settings
- Clinically, false positive results occur during pregnancy due to cross-reactivity with autoantibodies & alloantibodies
- Clinical, emotional, interpersonal, logistical reasons in favor and against treatment while awaiting PCR results (Figure 2)
- Point-of-care viral testing may be helpful, tailored strategy to confirm diagnosis in such limited cases
- Need for guidelines to clarify public health approaches for programs providing PrEP in pregnancy

Acknowledgements

We would like to acknowledge the PrIMA Study Staff and the Homa Bay and Biaaya County Directors of Health for their support on this project. We thank the Kizazi Working Group and University of Washington Global Center for the Integrated Health of Women, Adolescents, and Children, (Global WACH) for comments and insights provided during study design and manuscript development. Most of all, we thank the women and infants who have and will participate in the study.

Figure 1: World Health Organization and Kenyan national algorithm for HIV testing

Figure 2: Pros and cons of immediate treatment of women with discrepant results while awaiting PCR