Summary of Perinatal HIV Roundtable at CROI 2018

CROI 2018 * Boston, MA * March 6, 2018
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Topic

"Does U=U in the Perinatal HIV Setting? How do we talk to our patients about the 'Undetectable = Untransmittable' campaign and how it affects women, their partners, their infants, and their healthcare decisions?"

Background

The National Perinatal HIV Hotline (www.nccc.ucsf.edu) hosts discussions at CROI to build community among providers in our Perinatal HIV Clinicians Network and ReproID HIV listserv, and provide input on complex topics from the larger community of Perinatal HIV providers back to clinicians who staff the hotline. Discussion notes are distributed via the ReproID HIV listserv.

This year's topic, germinated by a question posted to the ReproID HIV listserv by Shannon Weber, Director of HIVE, focused on the 'Undetectable = Untransmittable' campaign and its relevance in the perinatal HIV setting, specifically breastfeeding.

Introduction

Over the last decade, a large body of evidence has accumulated supporting the effectiveness of sustained HIV viral suppression in preventing sexual transmission of HIV. Findings from several large studies have confirmed that the risk of HIV transmission from a person living with HIV who is taking antiretroviral therapy (ART) as prescribed and has achieved an undetectable viral load (VL) for at least six months is negligible to non-existent.[1] Additionally, there is strong evidence that women who are taking ART with an undetectable VL before conception and throughout pregnancy have "virtually zero" risk of transmitting the virus to their infant.[2] The transmission risk during breastfeeding is less clear due to fewer data, especially in high resource settings, coupled with concerns of heightened risk for transmission even in the setting of plasma suppression due to cell-associated HIV DNA in breast milk. British guidelines recommend against breastfeeding but the consultation draft of the British HIV Association 2018 guidelines on the management of HIV infection in pregnant women states: "Women who are virologically suppressed on [combination] ART with good adherence and who choose to breastfeed may be supported to do so, but should be informed about the low risk of transmission of HIV through breastfeeding in this situation."[3] Similarly, European guidelines advise against breastfeeding: "In case a woman insists on breastfeeding, we recommend follow-up with increased clinical and

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[1] U.S. Centers for Disease Control & Prevention (CDC), Dear Colleague Letter (September, 2017)
"Risk of Sexual Transmission of HIV from a Person Living with HIV who has and Undetectable Viral Load, Messaging Primer & Consensus Statement." *Prevention Access*, revised January 28, 2018. https://www.preventionaccess.org/consensus. Accessed 13 June 2018.

[2] Mandelbrot, L., Tubiana, R., Le Chenadec, J., et al. "No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception." *Clinical Infectious Diseases*, vol. 61, no. 11, 2015. pp. 1715–1725. DOI: 10.1093/cid/civ578.

[3] Gilleece Y., Tariq S., Bamford A., et al. British HIV Association guidelines on the management of pregnancy for women living with HIV. Consultation draft. Revised 2018. http://www.bhiva.org/documents/Guidelines/Pregnancy/2018/BHIVA-Pregnancy-guidelines-consultation-draft-final.pdf. Accessed 13 June 2018.

virological monitoring of both the mother and the infant."[4] The U.S. DHHS guidelines do not recommend breastfeeding, however in March 2018 the panel acknowledged that "women may face environmental, social, familial, and personal pressures to consider breastfeeding, despite the risk of HIV transmission via breast milk." Therefore guidelines were updated to provide tools to help providers counsel women on the potential risks associated with breastfeeding as well as a harm-reduction approach for women who choose to breastfeed despite counseling.[5] This grey area leaves providers with many questions about the best way to discuss these concepts with patients and families.

At the HIV and Women conference (http://www.virology-education.com/event/previous/international-workshop-hiv-women/) that preceded CROI, there was vibrant discussion about the challenges of the divergent guidelines for women who spend time in places with differing guidelines and for providers who want to support them. Given this discussion and the CROI 2018 symposium highlighting the many unknowns about viral transmission and infant outcomes with breastfeeding ("Breast is best, but it's a viral milkshake!")[6], we decided to focus this discussion on: (a) challenges to counseling women about formula feeding and breastfeeding, (b) strategies to support women in their choices, and (c) research priorities to help women, providers, and families with this challenge.

Lynn Matthews commented on her research in Uganda looking at women/breastfeeding and noted that women find it challenging to interpret different guidelines about breastfeeding.[7]

Judy Levison practices in Houston which has a large community of women from African countries such as Nigeria, who are surprised to hear that breastfeeding is discouraged. After one woman with a consistently undetectable VL expressed her plans to breastfeed despite counseling, Judy engaged her local pediatric infectious disease specialists, general pediatricians, and obstetricians to formulate a plan. This included the patient signing a consent to breastfeed and agreeing to monthly VL monitoring. Judy also noted that one potential pitfall of supporting some women to breastfeed is that non-specialist providers may miss the nuance and interpret this as an endorsement of breastfeeding for all women living with HIV. This highlights the importance of collaboration and communication.

The group then had a participatory and lively discussion.

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[4] European AIDS Clinical Society (EACS) Guidelines, version 9.0, revised October 2017. http://www.eacsociety.org/files/guidelines_9.0-english.pdf. Accessed 13 June 2018.

[5] Since CROI 2018, the U.S. DHHS Perinatal HIV guidelines section on breastfeeding was updated and can be found here: https://aidsinfo.nih.gov/guidelines/html/3/perinatal/513/counseling-and-management-of-women-living-with-hiv-who-breastfeed. Accessed 5 April 2018.

[6] CROI 2018. Abstract 52, 53, 54, and 55.

[7] Dunkley E., Ashaba S., Burns B., et al. "'I beg you…breastfeed the baby, things changed': infant feeding experiences among Ugandan mothers living with HIV in the context of evolving guidelines to prevent postnatal transmission." *BMC Public Health,* vol. 18, no. 1, 2018. pp. 188. DOI:10.1186/s12889-018-5081-x

Challenges:

- Multiple participants made the point that some patients will breastfeed regardless of provider counseling. The onus is on providers to create safe spaces to talk about real practices. Otherwise patients may breastfeed in secret or avoid care out of shame, guilt, or other feelings or considerations.
- There are still many unknowns around the risk of breast milk transmission: What counts as virologically suppressed or undetectable status for breastfeeding? How long does the maternal VL need to be undetectable? What level of detection? How do we (and our patients) understand and interpret the risk of transmitting HIV to a breastfeeding infant? Comments were made that lack of knowledge about the grading of the risks made it impossible to dismiss the risk completely.
- Patients are aware of the differences in recommendations on breastfeeding between global and national guidelines – some women travel between countries during pregnancy and between pregnancies, others may just read the various guidelines. It's confusing that in-country guidelines change over time and that guidelines differ between countries. In addition, women often have friends and family and local providers in countries with different guidelines and hear contradictory recommendations. This is confusing and also undermines the value of the guidelines/highlights the unknowns.
- We know that postpartum adherence to visits and ART is often very challenging for women. Is there a way to predict who will fall out of care and/or stop taking ART? Are there ways to provide additional support? Would breastfeeding women be more engaged in care and more motivated to maintain an undetectable VL for the health of her infant?
- There is no consensus on management and monitoring of breastfeeding women with HIV and their infants in high resource settings. Practices vary widely. Because this is still a largely unsanctioned practice, there is not a lot of communication among providers who are managing breastfeeding women with HIV and their infants. Some providers may feel nervous sharing their practices/experiences. We need safe spaces for providers, too.
    - There is a need for evidence-based guidance on infant prophylaxis/testing: What ART option(s)? Duration? How to monitor, both for transmission and for toxicity?
    - Pediatric testing can require larger blood volumes that are challenging to obtain – should monitoring focus on mother, infant, or both?
    - Some providers do VL monitoring of the breast milk, but not all labs will perform VL testing on breast milk.
    - Parents often experience stress and anxiety throughout the follow up/testing period.
    - Exclusive breastfeeding is recommended for women with HIV, but how often is it practiced in the U.S.? In reality, providers often don't know all the details of how families are feeding babies.
    - What to do if a breastfeeding woman has a VL that comes back elevated?
- Women living with HIV and HIV-exposed infants often benefit from interdisciplinary care. That need is even more relevant in the case of a woman who is breastfeeding. However, adult infectious disease, obstetrics, pediatric infectious disease, general pediatric, and other provider disciplines are not necessarily on the same page in terms of comfort with breastfeeding and preferences for monitoring and prophylaxis. It is essential to identify an interdisciplinary strategy/approach that effectively supports women and their families.

Strategies:

- Reframe the conversation: We are not "letting" patients breastfeed, they might breastfeed with or without us. We are supporting our patients to more safely breastfeed and lower the risk of HIV transmission to infants.
- Allow for open and honest conversations around infant feeding that will allow patients/families to make informed decisions with the best information available. It is important to promote trust and approach each patient situation with a lack of judgment.
- Use open-ended questions to help women discuss their thinking (e.g. "What are your thoughts on feeding?" instead of "You can't breastfeed." or "You need to formula feed.") Leave space for questions (e.g. "What questions do you have about what we've discussed so far?").
- Supporting women in their infant feeding decision also requires explicitly supporting women who choose to formula feed.
    - Some patients don't want to breastfeed, despite family and social pressures, and are relieved to be told that they can and should formula feed.
    - When the pressure to breastfeed is external, providers can help patients formulate non-HIV-related reasons/responses to share with friends and family for why they are not breastfeeding. One proposal is mothers who tell their families that the pain medication they received in labor will be "in their system" for a long time, and therefore they were advised not to breastfeed. Such approaches may be particularly helpful for women who have not disclosed their HIV status.
    - Support women's access to infant formula through WIC and other programs.
    - Stress the importance of choosing either breastfeeding or formula feeding in order to discourage mixed feeding.
    - Participants shared anecdotes of women living with HIV in low- and middle-income countries who had the resources and wanted to formula feed, but were told that the best and only option was to breastfeed. These women also felt like they were denied the opportunity to make their own informed decisions.
- Some providers find it helpful to use scripts and contracts in conversations with patients who choose to breastfeed. Others find contracts to be overly medico-legal and stigmatizing of the practice of breastfeeding. It is important to have clear and thorough documentation of discussions with patients.
- Breastfeeding for a shorter period of time – just the first few weeks – might allow some women to bond with their infant the way they want to, and then they can transition to formula feeding.
- There are multiple approaches to infant prophylaxis, without any studies designed to compare these approaches head to head. Some providers feel comfortable with just standard AZT prophylaxis for 4-6 weeks with a focus on ART and VL monitoring for the breastfeeding woman without additional prophylaxis for her infant. Other providers add NVP starting at birth and continued until one month after weaning. Some providers reported feeling only comfortable with a three-drug combination of AZT/3TC/NVP as post-exposure prophylaxis (PEP) for infant throughout the breastfeeding duration.
- Monitoring strategies also vary, but generally entail some strategy for more intensive monitoring during breastfeeding (providers discussed breast milk VL testing, monthly infant VL testing, monthly maternal VL monitoring) as well as a strategy for follow up infant testing (one suggestion was testing at 1, 2, 4, and 6 months after weaning).
- Participants discussed how to respond to a detectable maternal VL: start or expand PEP for the infant, repeat maternal VL to determine if it's a blip or impending/persistent virologic failure, infant

testing, counsel to hold breastfeeding (at least until maternal VL returns to undetectable), and/or perhaps stop completely.
- Breastfeeding with HIV requires high levels of support and coordination, and should involve labor and delivery nurses; OB, ID, adult, and pediatric providers; inpatient and outpatient providers; lactation consultants; case managers; and likely others. A plan for exclusive breastfeeding, ART adherence (maternal and infant), and weaning should be made in advance with input from all.

Areas for Further Research:

- Study adherence in breastfeeding women – there may be an emerging role for [hair] drug concentration testing to monitor adherence. Are there validated tools to predict adherence? Are there ways to support women?
- What is the best follow up strategy for women/infants?
- What are the long-term impacts of ART given during infancy or absorbed through breastfeeding? (Create a breastfeeding registry similar to the Antiretroviral Pregnancy Registry)
- Does the infant also need prophylaxis? PrEP vs. PEP vs. none? AZT vs. NVP vs. both (or other) for the first 6 weeks?
- What is the risk of HIV transmission through breastfeeding in high resource setting? What about with ART started early in (or prior to) pregnancy? What about long term (i.e. years) viral suppression?
- What is the significance of breast milk cell-associated virus vs. free virus? How do blips in maternal serum VL correlate with breast milk viremia? How should we interpret breast milk viremia in the absence of viremia in the blood?
- Creation and validation of tools for shared decision making regarding infant feeding
- Ethics: Some providers expressed concern about whether it is ethically appropriate for women to choose to breastfeed when living with HIV given the many unknowns. What is a provider's ethical obligation/role and own ethical/moral position?

Ideas for Next Steps:

- Create a registry and/or case series to start discussing the issues and challenges outlined above and help engender support/tools/research
    - **Contact Judy Levison (jlevison@bcm.edu) with your cases of women who are breastfeeding with HIV**
- Keep the conversation going across disciplines
- Regular teleconferencing/virtual roundtables on the topic
- Workshops
- Antiretroviral breastfeeding registry
- Cross-national data collection and collaboration
- Develop and disseminate counseling tools
- Collaborative statement outlining challenges and major research issues/gaps in care/unmet needs
- Set up a separate listserv or online discussion forum
- Host a conference on infant feeding and HIV, or hold a conference track/session on the topic

The following are topics that were brought up during the discussion but, due to lack of time, couldn't be fully discussed:

- Switzerland → no infant PEP after delivery for undetectable VL, vaginal delivery
- One participant shared a story of a patient who tested negative for HIV during pregnancy, and then seroconverted while she was breastfeeding, resulting in transmission of HIV to her infant: How can we identify/monitor/follow up/support women without HIV who are at risk for acquiring HIV during breastfeeding? Is there a role for routine 4th generation Ag/Ab testing in high prevalence areas during breastfeeding?

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Discussion notes are distributed via the ReproID HIV listserv. The ReproIDHIV Listserv is a dynamic forum for clinicians and other healthcare professionals who specialize in reproductive infectious diseases. Participants use the forum to discuss clinical cases, share clinical approaches and protocols, network with colleagues, and arrange patient referrals. For more information, or to join the listserv, please contact marliese.warren@ucsf.edu.

As always, we are stronger together and there are many people who contribute to the success of our annual Perinatal HIV Roundtable. In no particular order, we want to offer our gratitude to:

Betty Dong
Ron Goldschmidt
Carolyn Chu
Brenda Goldhammer
Deb Cohan
Shannon Weber
Judy Levison
Lynn T. Matthews
Lealah Pollock
Christine Pecci
Pooja Mittal
Peter Havens
Ted Ruel
Marliese Warren
IAS-USA Conference Organizers

The entire ReproID HIV Listserv and greater perinatal and pediatric HIV communities

Attendees – CROI 2018 Perinatal HIV Roundtable	
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