ARV Adherence Associated with Reduced Breastmilk HIV Viral Load and HIV Transmission (#886)

Nicole L. Davis[1], William C. Miller[1], Michael G. Hudgens[1], Charles S. Chasela[2], Dorothy S. Sichali[3], Julie A.E. Nelson[1], Joseph Rigdon[1], Sascha R. Ellington[4], Athena P. Kourtis[4], Charles M. van der Horst[1]

[1]University of North Carolina at Chapel Hill, NC, [2]University of Witwatersrand, Parktown, South Africa, [3]University of North Carolina Project, Lilongwe, Malawi,[4]Centers for Disease Control and Prevention, Atlanta, GA

BACKGROUND

To prevent mother-to-child HIV transmission (PMTCT), antiretroviral (ARV) interventions are used to reduce HIV viral replication in breastmilk and maternal blood.

Achieving and maintaining viral suppression relies on adherence to ARV regimens.

OBJECTIVES

1. Quantify the association between:
   - ❖ Adherence to postpartum maternal combination ARVs and breastmilk HIV viral load
   - ❖ Plasma HIV viral load and breastmilk HIV viral load
   - ❖ Breastmilk HIV viral load and HIV transmission
2. Estimate the number of additional infant infections averted with perfect maternal ARV adherence

STUDY POPULATION

The BAN Study: Randomized trial in Lilongwe, Malawi (2004-2010) to assess the benefit and safety of ARVs given to HIV-infected mothers or their infants to prevent breastmilk HIV transmission.

Select BAN eligibility criteria:
- ❖ Maternal HIV infection with CD4 ≥ 250
- ❖ No prior ARV use, including single-dose nevirapine (NVP)

Analysis eligibility criteria:

Mother-infant pairs with ≥1 plasma or breastmilk specimen 2-24 weeks postpartum, randomized to:
- ❖ 28 weeks of combination antiretrovirals given to mother only (ZDV+3TC+ either LPV/r, NFV, or NVP)
- ❖ 28 weeks of daily NVP given to infant only

Among those:
- ❖ All mothers who transmitted HIV to their infant 2-28 weeks postpartum (n=31, 94% of transmission events)
- ❖ 15% of mothers who did not transmit by 28 weeks (n=232)

Table 1. Odds ratios for adherence and detectable (≥40 copies/ml) plasma HIV RNA as a risk factor for detectable (≥56 copies/ml) breastmilk HIV RNA.

	Complete case				Imputed			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	Odds Ratio	(95% CI)	Odds Ratio	(95% CI)	Odds Ratio	(95% CI)	Odds Ratio	(95% CI)
Exposure: Adherence								
Maternal and Infant Arm								
>80-98% adherent vs 0-80%	0·24	(0·08, 0·72)	0·23*	(0·08, 0·67)	0·30	(0·07, 1·30)	0·29*	(0·07, 1·19)
>98% adherent vs 0-80%	0·38	(0·17, 0·86)	0·36*	(0·16, 0·81)	0·42	(0·10, 1·83)	0·41*	(0·10, 1·69)
Maternal arm only								
>80-98% adherent vs 0-80%	0·47	(0·16, 1·41)	0·47*	(0·15, 1·40)	0·50	(0·11, 2·21)	0·50*	(0·11, 2·21)
>98% adherent vs 0-80%	0·64	(0·28, 1·43)	0·64*	(0·29, 1·43)	0·67	(0·15, 2·96)	0·68*	(0·15, 3·00)
Exposure: Plasma HIV RNA								
Maternal and Infant Arm								
Detectable vs. Undetectable	59	(21, 169)	40**	(15, 107)	43	(8, 236)	35**	(7, 169)
Maternal arm only								
Detectable vs. Undetectable	45	(16, 124)	40**	(15, 108)	41	(9, 185)	38**	(9, 168)

* Adjusted for: baseline maternal age, CD4+ count and $\log_{10}$ plasma viral load, as well as nutritional randomization.

**Adjusted for: baseline maternal CD4+ and baseline maternal plasma viral load. Study arm was included as a confounding variable in combined maternal and infant arm models, but was not included in maternal arm only models.

Table 2. Odds ratios for detectable (>56 copies/ml) breastmilk HIV RNA as a risk factor for breastmilk HIV-1 transmission.

	Complete Case				Imputed			
	Unadjusted*		Adjusted**		Unadjusted*		Adjusted**	
	Hazard Ratio	(95% CI)	Hazard Ratio	(95% CI)	Hazard Ratio	(95% CI)	Hazard Ratio	(95% CI)
Maternal and Infant Arm								
Detectable vs. Undetectable	2·7	(1·4, 5·4)	7·4	(3·2, 17·1)	2·9	(1·0, 8·4)	3·8	(1·2, 12·1)
Viral load by study arm								
Maternal ARV: Detectable vs. Undetectable	5·6	(2·5, 12·7)	7·8	(3·1, 19·2)	4·8	(1·5, 15·8)	4·4	(1·3, 15·2)
Infant NVP: Detectable vs. Undetectable	3·9	(0·8, 18·0)	6·0	(1·2, 31·4)	2·8	(0·5, 15·0)	2·9	(0·5, 17·7)

*Combined maternal and infant arm models contained no confounding variables. Viral load by study arm models contained study arm and an interaction term between breastmilk viral load and study arm.

**Adjusted for continuous baseline maternal age, baseline maternal CD4+, baseline maternal hemoglobin level, and baseline maternal plasma viral load. Study arm was included as a confounding variable in combined maternal and infant arm models. Viral load by study arm models included an interaction term between breastmilk viral load and study arm.

ANALYSIS

Adherence was measured using maternal ARV pill counts and categorized as poor (0-80%), partial (81-98%) and near perfect (>98%).

Mixed effects models were used to estimate the associations between: 1) maternal ARV adherence and breastmilk HIV viral load, and 2) plasma HIV viral load and breastmilk HIV viral load.

Cox models were used to estimate associations between breastmilk HIV viral load and breastmilk HIV transmission 2-28 weeks postpartum.

Monte Carlo simulation was conducted to estimate the additional number of transmissions that would have been averted between 2-28 weeks postpartum if all mothers randomized to maternal ARVs (n=848) had been 100% adherent.

RESULTS

Having partial or near perfect ARV adherence significantly reduced the odds of having detectable (≥40 copies/ml) breastmilk RNA, compared to poor adherence (OR 0·23, 95% CI 0·08-0·67; OR 0·36, 95% CI 0·16-0·81, respectively).

Detectable breastmilk RNA was associated with 7·4 (95% CI 3·2-17·1) times the adjusted relative rate of breastmilk transmission, compared to undetectable breastmilk RNA.

Among mothers who transmitted HIV to their infant, all had at least one plasma viral load >100 copies/ml.

Using Monte Carlo simulation, if all mothers randomized to maternal ARVs had been 100% adherent we estimated an additional 33% decrease in HIV transmissions between 2-28 weeks postpartum, compared to transmissions under observed adherence.

CONCLUSIONS

Better adherence was associated with lower breastmilk RNA, and lower breastmilk RNA was associated with a lower risk of transmission. An estimated additional 33% of transmissions could have been averted with perfect maternal ARV adherence.

Maintaining plasma viral load <100 copies/ml may be effective at preventing breastmilk transmission.

National Center for Chronic Disease Prevention and Health Promotion
Division of Reproductive Health

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