1077BF: Breast Milk Reservoir, Tenofovir levels and HIV Transmission Among Breastfeeding Mothers

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IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network

PROMISE IMPAACT 1077

Promoting Maternal and Infant Survival Everywhere

BACKGROUND

- Recent studies observed detectable HIV-1 virus levels in breastmilk (BM) despite undetectable HIV-1 RNA viral load (VL) in plasma.
- This discordance could account for residual vertical HIV-1 transmission during lactation.
- **We assessed the association of vertical HIV-1 transmission with HIV VL in plasma and BM, and with plasma and BM tenofovir (TFV) concentrations.**

METHODS

- Nested case-control postpartum substudy within the IMPAACT PROMISE 1077BF perinatal HIV trial, which compared randomized ARV strategies to prevent perinatal HIV transmission including during breastfeeding.
- Cases: mother-infant pairs with infants who had a positive HIV nucleic acid test (NAT) during the breastfeeding period; Controls: mother-infant pairs with infants who were HIV NAT negative.
- 1:2 matching by infant sex, study site, maternal age at delivery, and 1077BF postpartum (PP) component during breast feeding.
- Maternal plasma and BM collected near an infant's infection date were assayed for HIV total nucleic acid (TNA; DNA + RNA) VL, DNA VL, RNA VL, and TFV concentration.
- Conditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CI).

TABLE 1. Baseline Characteristics

Characteristic[1]	Cases	Controls
	(n=31)	(n=62)
Maternal age at delivery (years)	24 (22, 27)	25 (22, 27)
Randomized in PP Component[2]	19 (61%)	38 (61%)
Plasma HIV-1 RNA VL (log_{10} copies/mL)	5 (4, 5)	4 (3, 4)
Infant sex (male)	13 (42%)	26 (42%)
Gestational age at birth (weeks)	38 (36, 40)	39 (38, 40)

[1]Continuous variables are summarized as median (Q1, Q3); Categorical variables are summarized as n (%).
[2]Mother-infant pairs were randomized in the PP Component to maternal ARVs (TFV-based) or infant prophylaxis. Mother-infant pairs not randomized in the PP Component (39%) were in antepartum (AP) long-term follow-up.

The ***odds of infant HIV acquisition*** were ***2.6 times higher*** for each log_{10} increase in maternal plasma RNA viral load and ***1.8 times higher*** for each log_{10} increase in maternal breastmilk RNA viral load.

TFV levels for mothers whose infants acquired HIV were **lower** compared with mothers whose infants didn't acquire HIV: ***10-fold lower for plasma a***nd ***5-fold lower for breastmilk*** .

RESULTS

- 93 mother-infant pairs (31 cases; 62 controls) from Malawi, Uganda, South Africa, Zimbabwe, and India were included.
- Median (Q1, Q3) age of infant infection was 6 (3, 14) months. Over 70% (22/31) of samples were taken on the same day or within one month of infection.

HIV-1 Viral Load

- Median (Q1, Q3) maternal plasma VL was 39,228 (4822, 124,886) copies/ml for cases vs 20 (20, 2,104) for controls (Figure 1).
- BM RNA VL was above lower limit of quantification for 17 (55%) cases vs 7 (11%) controls.
- The odds of infant HIV infection were 2.6 times higher for each log_{10} increase in maternal plasma RNA VL (95% CI: 1.6-4.5) and 1.8 times higher for each log_{10} increase in maternal BM RNA VL (95% CI: 1.3-2.6).

TFV Concentration

- Only 3/14 (21%) case mothers on a TFV-containing regimen had detectable TFV levels in their plasma or BM vs 31/37 (84%) control mothers with detectable TFV in plasma and 29/37 (78%) in BM (Figure 2).
- Plasma TFV concentrations were 10-fold lower [geometric mean ratio (95% CI): 0.11 (0.04-0.26)] in cases compared with controls, and BM TFV concentrations were 5-fold lower [GMR (95% CI): 0.18 (0.08-0.43)] in cases compared with controls.

CONCLUSIONS

In this PROMISE 1077BF nested case-control study, higher maternal plasma and BM VL and lower TFV concentrations was associated with higher odds of postpartum breastmilk HIV-1 transmission .

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FIGURE 1. HIV-1 VL by case-control status

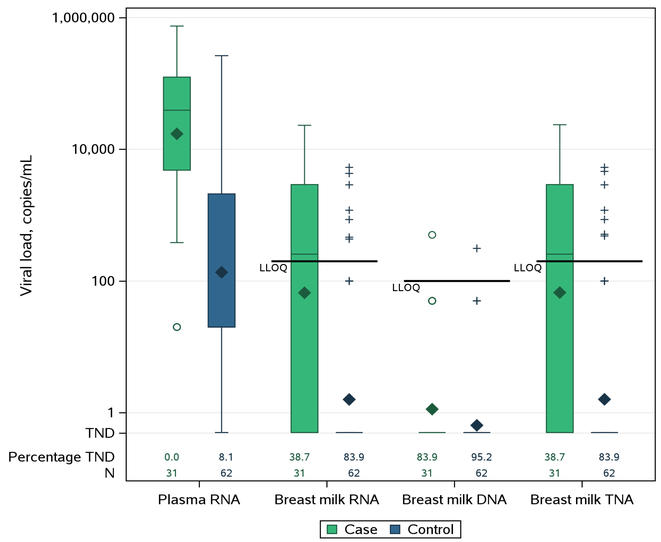
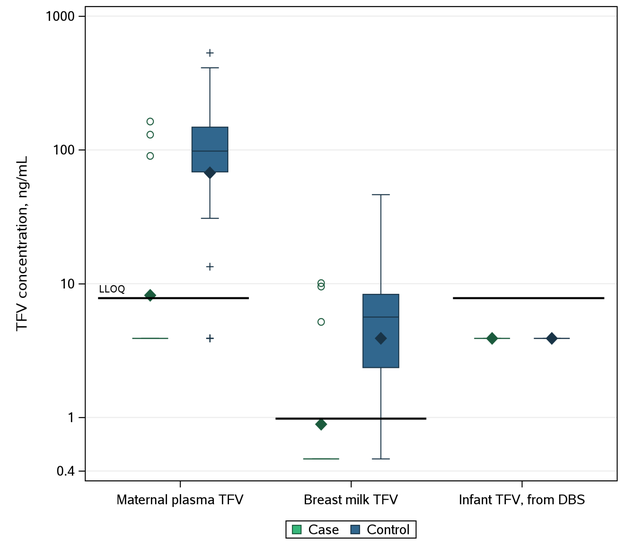


FIGURE 2. TFV concentration by case-control status



Lower limit of quantification (LLOQ) was 20-400 copies/mL for plasma RNA VL, 200 copies/mL for breastmilk RNA VL, 100 copies/mL for breastmilk DNA VL, 200 copies/mL for breastmilk TNA VL, 7.8 ng/mL for plasma and DBS TFV, and 0.98 ng/mL for breast milk TFV. Target not detected (TND) was imputed as 0.5 copies/mL. Diamond represents mean, thin horizontal line represents median, thick black line represents LLOQ.

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