Maternal antiretroviral therapy in pregnancy and neonate pre-treatment viral load

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Abstract

Background: With expansion of effective maternal antiretroviral therapy (ART), rates of new infant infections are low but a large proportion of infected infants are exposed to ART before birth. We investigated relationships between maternal ART in pregnancy and pre-treatment (PT) viral load (VL) profiles in intrauterine-infected neonates.

Methods: Between June 2014 and December 2017, 99 neonates with confirmed HIV-infection were identified through a birth testing program at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa, and had a PT VL available in the neonatal period . VL was measured using the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 test, version 2.0 (Roche Molecular Systems, Inc., Branchburg, NJ). Maternal VL's were measured during late pregnancy, at delivery or soon thereafter using the same assay.

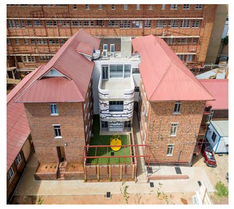
Results: Of the 99 intrauterine-infected neonates, 51.5% were female, mean birthweight was 2,846 ± 553 grams and 87.9% were ≥37 weeks of gestation. 14.3% of mothers first learned their HIV status during admission for this delivery, 53.1% during this pregnancy, and 32.7% prior to this pregnancy. 19.2% of mothers received no ART before delivery, 28.3% <12 weeks and 50.5% >12 weeks of ART. All infants were given NVP prophylaxis prior to diagnosis. 95 infants (96%) had a VL measured in the neonatal period. This VL measurement took place prior to starting ART for all but four children ,these were excluded from the analysis. Neonate PT VL was measured at a median of 1 day (IQR 1 - 7) with a median of 25,091 copies/ml (cpm) (IQR 2,045 - 216,305) and 19.8% had a VL<1,000 cpm. Neonate PT VL was correlated with maternal VL (r=0.58, p<0.01). Neonate PT VL was significantly (p<0.01) lower (median 801 cpm) among those whose mothers received ART and had a maternal VL<1,000 cpm than among those whose mothers reported receipt of ART but with VL>1,000 cpm (median 35,071 cpm) or among those whose mothers had received no ART (median 48.905 cpm). Among neonates with PT VL<1,000 cpm, 55.6% had mothers on ART with maternal VL<1,000 cpm compared to 13.7% among neonates with PT VL>1,000 cpm (p=0.0001).

Conclusion: Most (>80%) mothers received ART during pregnancy. The lowest neonate PT VLs were observed in neonates whose mothers adherence to and duration of ART led to maternal VL<1,000. Pre-treatment viral load in these intrauterine-infected neonates correlated significantly with maternal viral load.

Introduction

- Maternal VL is a risk factor for the mother-to-child transmission of HIV.
- Maternal VL may have implications for VL in the neonate and may lead to a reduction in the size of the viral reservoir.
- Recently a decline in neonatal VL levels in South Africa between 2010 and 2016 has been described. This has been attributed to increasing efforts to prevent mother to child transmission (PMTCT) with increasing both the number and duration of maternal ART's in pregnancy and the post partum period. WHO PMTCT regimen Option B+ was implemented in South Africa in 2015.
- We investigated relationships between maternal ART in pregnancy and PT VL profiles in intrauterine-infected neonates.

Methods



- We included 99 infants with confirmed HIV-infection identified through a universal birth testing program and enrolled onto a study protocol at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa between June 2014 and Dec 2017.
- Mothers or legal guardians signed written informed consent for their own and their infant's participation. The protocol was approved by the Institutional Review Boards of Columbia University in New York and the University of the Witwatersrand in Johannesburg.
- Quantitative HIV RNA VL was measured using the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 test, version 2.0 (Roche Molecular Systems, Inc., Branchburg, NJ). Neonate PT VL was defined as a VL measurement in the neonatal period (first 28 days of life) before ART was initiated.
- Maternal VL's were measured during late pregnancy, at delivery or soon thereafter using the same assay. Other clinical characteristics were obtained through examination and record review.

Results

- Of the 99 infants, 51.5% were female, mean birthweight was 2,846 ± 553 grams and 87.9% were assessed as having a gestational age ≥37 weeks.
- 14.3% of mothers first learned their HIV status during admission for this delivery, 53.1% during this pregnancy, and 32.7% prior to this pregnancy.
- 19.2% of mothers received no ART before delivery, 28.3% <12 weeks of ART during pregnancy, and 50.5% ≥12 weeks of ART during pregnancy.
- 95 infants (96%) had a VL measured in the neonatal period. This VL measurement took place on, or prior to the day of starting ART for all but four children (these had VL's done at 3, 5, 11, and 13 days after ART initiation). These four were excluded from additional analyses in **Table 1**.
- 17 mothers had no ART until delivery, 74 did have ART and majority (52.7%) of those had more than 12 weeks of ART before delivery.

Table 1: Maternal ART initiation and VL's by maternal category

Characteristic	No ART (N=17)	Any ART (N=74)
ART during this pregnancy, N (%)		
Yes, started before pregnancy and cont.	0 (0.0)	15 (20.3)
Yes, during pregnancy, ≥12 weeks of ART	0 (0.0)	24 (32.4)
Yes, during pregnancy, <12 weeks of ART	0 (0.0)	33 (44.6)
Yes, during pregnancy, unknown when started	0 (0.0)	2 (2.7)
No ART up until delivery	17 (100.0)	0 (0.0)
Maternal viral load (copies/ml), N (%)		
<1,000	2 (11.8)	20 (27.0)
≥1,000	15 (88.2)	54 (73.0)
Maternal viral load (copies/ml), Median (IQR)	81,517 (15,100 – 143,000)	29,815 (608 – 97,473)

- Neonate PT VL was measured at a median age of 1 day (IQR 1 – 7) with a median of 25,091 cpm(IQR 2,045 – 216,305) and 19.8% had a VL<1,000 cpm.
- All 91 infants had a maternal VL measurement available. Maternal VL was measured at a median infant age of 1 day (IQR 1 – 6) with a median of 33,037 cpm (IQR 1,002 – 104,538) and 24.2% had a VL<1,000 cpm.
- Neonate PT VL was significantly correlated with maternal VL (r=0.58, p<0.01) (**Figure 1)**.

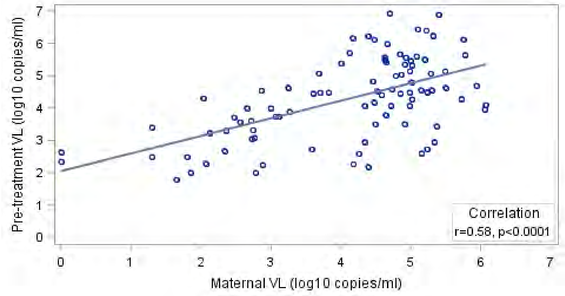


Figure 1: Infant pre-treatment viral load compared to maternal viral load.

- Maternal VL was higher in the 17 mothers who received no maternal ART (median 81,517 cpm, IQR 15,100 – 143,000) compared to 74 who reported any ART (median 29,815 cpm, IQR 608 – 97,473 cpm)(**Figure 2**).

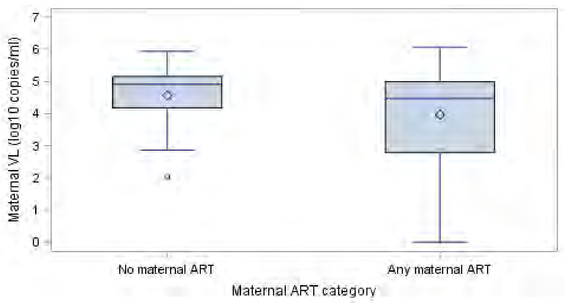


Figure 2: Maternal viral load by maternal ART status

- Neonate PT VL was significantly lower (median 801 cpm) among those whose mothers reported receiving ART and had a maternal VL<1,000 cpm than among those whose mothers reported receipt of ART but with VL ≥1,000 cpm (median 35,071 cpm) or among those whose mothers had received no ART (median 48,905 cpm) **(Figure 3)**.

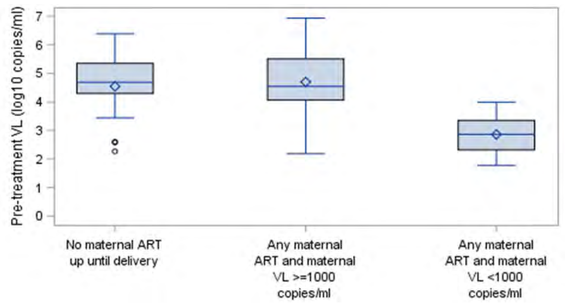


Figure 3: Neonate pre-treatment viral load by maternal ART category

Table 2: Neonate pre-treatment viral load by maternal ART category with comparative p-values

	Group 1: No maternal ART up until delivery (N=17)	Group 2: Any maternal ART and maternal VL ≥1000 cpm (N=54)	Group 3: Any maternal ART and maternal VL <1000 cpm (N=20)	P-value
Neonatal PT VL (cpm), Median (IQR)	48,905 (19,825 – 224,515)	35,071 (11,600 – 320,125)	801 (208 – 2,280)	All: <0.0001 1 vs. 2: 0.94 2 vs. 3: <0.0001 1 vs. 3: 0.0001

- Among neonates with PT VL<1,000 cpm, 55.6% had mothers on ART with maternal VL<1,000 cpm compared to 13.7% among neonates with pre-treatment VL ≥1,000 cpm (p=0.0001).
- Correlations of neonate PT VL and maternal VL by maternal ART status are shown in **Figure 4 and 5**.

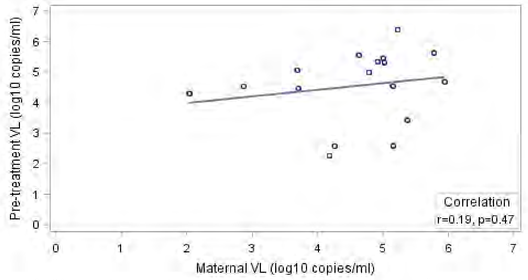


Figure 4: Neonate pre-treatment viral load compared to maternal viral load in the no maternal ART group

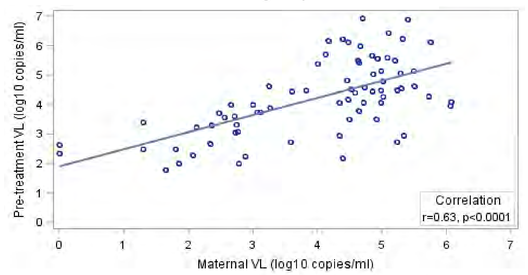


Figure 5: Neonate pre-treatment viral load compared to maternal viral load in the any maternal ART group

Conclusions

- Pre-treatment viral load in these intrauterine-infected neonates was lower than expected and correlated significantly with maternal viral load.
- Intra-uterine infected neonates born to mothers that received ART during pregnancy (>80%) and that sustained viral suppression (VL<1000 cpm) had significantly lower PT VL's compared to those born to mothers that received no ART prior to delivery or did not suppress the virus.
- Maternal ART during pregnancy may begin treatment of intrauterine infection.

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