Maternal antiretroviral therapy in pregnancy and neonatal VL load

Faeezah Patel1, Stephanie Shiau1,4,5, Renate Strehlau1, Megan Burkle1, Martie Conradie1, Maria Paximadis2, Sharon Shalekoff2, Diana Schramm2, Caroline Tiemessen2, Elaine J. Abrams1,4,5,6, Gayle Sherman1,2, Ashraf Coovadia1, Louise Kuhn1,3,4, on behalf of the LEOPARD study team.

1. Employees Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa;
2. Centre for HIV and STIs, National Institute for Communicable Diseases, Johannesburg, South Africa, South Africa;
3. Gertrude H. Sergievsky Centre, College of Physicians and Surgeons, Columbia University, New York, NY, USA;
4. Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA;
5. ICAP at Columbia, Mailman School of Public Health, Columbia University, New York, NY;</div>

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 prophylaxis prior to delivery. 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, who were excluded from the analysis.

Maternal VL was measured at a median of 1 day (IQR 3-7) with a median of 25,091 copies/ml (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 81,517 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.

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 December 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 and 50.5% >12 weeks of ART. All infants were given prophylaxis prior to delivery.

• 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, who were excluded from the analysis.

• Neonate PT VL was measured at a median of 1 day (IQR 3-7) with a median of 25,091 copies/ml (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 81,517 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 pre-treatment VL<1,000 cpm (p=0.0001).

• Correlations of neonate PT VL and maternal VL by maternal ART status are shown in Table 2. Figure 4 shows the relationship between maternal ART status and neonatal VL. Figure 5 shows the relationship between maternal ART status and neonatal VL by maternal ART status.

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

<table>
<thead>
<tr>
<th>Group 1: No maternal ART (N=17)</th>
<th>Group 2: Any maternal ART up until delivery (N=74)</th>
<th>Group 3: Any maternal ART and maternal VL &lt;1,000 cpm (N=54)</th>
<th>Group 4: Any maternal ART and maternal VL ≥1,000 cpm (N=20)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate PT VL (log10 cpm), Median [IQR]</td>
<td>3.73 [3.25-4.13]</td>
<td>3.50 [3.10-4.00]</td>
<td>3.30 [3.00-4.00]</td>
<td>3.45 [3.00-4.00]</td>
</tr>
<tr>
<td>No maternal ART vs maternal ART up until delivery: 0.94</td>
<td>0.94 vs &lt;1,000 cpm: 0.94</td>
<td>0.94 vs ≥1,000 cpm: 0.94</td>
<td>0.94 vs maternal ART only: 0.94</td>
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<td>0.94 vs maternal ART only: 0.94</td>
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<tr>
<td>Neonate PT VL vs maternal VL: 1 vs 3: 0.0001</td>
<td>1 vs 2: 0.94</td>
<td>1 vs 3: &lt;0.0001</td>
<td>1 vs 2: &lt;0.0001</td>
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</tbody>
</table>

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 compared to those born to mothers that received ART prior to delivery or did not suppress the virus.

• Maternal ART during pregnancy may begin treatment of intrauterine infection.

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