Very early seroreversion among infants exposed to HIV in the era of effective maternal ART

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The challenge of **HIV diagnosis in infants**

- The diagnosis of HIV in infants requires molecular testing, as infants born to women living with HIV receive passive transfer of maternal HIV antibodies, which persist after birth and are detectable by serological assays.
- Current guidelines recommend against antibody testing for diagnosing infants ≤18 months of age due to the persistence of maternal antibodies.
- These guidelines are based on historical cohorts of HIV-exposed infants, in which the timing of maternal antibody clearance ranged from 7 months to as late as 24 months of age.

STUDY RATIONALE

- The dynamics of maternal HIV IgG decay in infants exposed to HIV during pregnancy have not been studied in recent cohorts of women who initiated ART prior to conception and maintained long-term viral suppression.
- We hypothesize that these women living with HIV (WLWH) may have lower circulating HIV antibody levels, resulting in reduced transplacental transfer of maternal HIV antibodies and faster seroreversion among exposed infants.

OBJECTIVES

1.To describe the timing of seroreversion among HIV-exposed infants in the *Centre maternel et infantile cohort.*
2.To identify biological and clinical factors associated with early seroreversion (< 5 months).

METHODS

- Prospective study of WLWH and their infants enrolled in the *Centre maternel et infantile sur le SIDA* (Montreal, Canada), 2018–2024.
- Women were enrolled at the first pregnancy visit, and their infants were followed from birth until 5 years of age.
- HIV-negative status was confirmed in exposed infants by at least two negative HIV DNA PCR tests performed at age ≥1 month and one at age ≥4 months. (HEU infant : HIV exposed uninfected infant.)
- HIV IgG antibody testing was performed at 1, 2, 4–6, and 24 months of age using the Biolytical INSTI HIV-1/HIV-2 assay (Se 99,8% , Spe 99,5%).

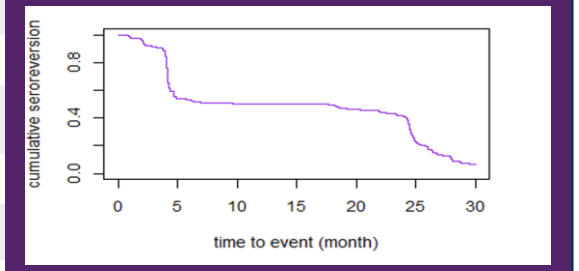
EARLY SEROREVERSION WAS DEFINED AS INFANT SERONEGATIVITY PRIOR TO 5 MONTHS OF AGE

Early seroreversion occurred in >30% of HEU infants and was associated with continuous viral suppression during pregnancy and preconception ART

Table 1 Charateristics of patients (n=241 mother-infant pairs)

WLWH age (years)	33.5 [30.7-37.3]
Time of WLWH diagnosis (years)	6.6 [3.0-10.9]
WLWH viral load < 20 cp/ml throughout pregnancy	65% (156/241)
At the time of delivery	
WLWH CD4 count (cells/mm^3)	576 [420-810]
WLWH CD8 count (cells/mm^3)	655 [460-863]
WLWH CD4/CD8 ratio	0.95 [0.63-1.40]
WLWH viral load < 20 cp/ml	89% (215/241)
WHIV initiated ART	
Prior to conception 1^{rt} Trimester 2nd Trimester 3rd Trimester	75% (185/241) 7.4% (18/241) 10.3% (25/241) 4.1% (10/241)
WHIV ART core	
II IP NNRTI	75% (182/241) 12% (29/241) 11% (27/241)
Birth term (WA)	39 [38.2 -39.6]
Birthweight (kg)	3.21 [2.9-3.5]
Breastfeeding	2.4% (6/241)

Figure 1: Time to seroreversion among all infants (n=241)

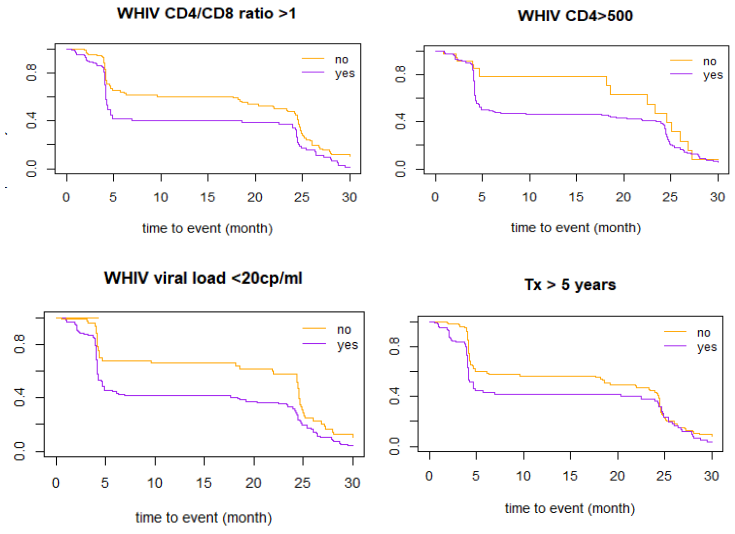


Time to seroreversion (month, med,IQR)	**4.1 [4.0-23.9]**
Seroreversion by 1 month	2.5% (6/241)
Early seroreversion (< 5 months)	**38% (91/241)**

Table 2: Factors associated with early seroreversion

Maternal CD4/CD8 ratio >1	OR 2.46 [1.3-4.7]	**p=0.004**
WLWH viral load < 20 cp/ml throughout pregnancy	OR 2.45 [1.2-4.9]	**p=0.006**
Treatment duration > 5 years	OR 2.0 [1.0-1.4]	**p=0.02**
WLWH CD4 > 500 at delivery (cells/mm^3)	OR 2.7 [0.9-9.0]	p=0.05
WLWH viral load < 20 cp/ml at delivery	OR 2.2 [0.6-8.7]	p=0.18
Pre-term birth (<37 WA)	OR 1.99 [0.4-12.7]	p=0.49

Figure 2 : Factors associated with early seroreversion



x-axe : time to seroreversion (month), y axe: event seroreversion

CONCLUSIONS

- Early seroreversion occurred in nearly 1/3 of HIV-exposed uninfected infants, with **some infants seronegative by 1 month of age**.
- Early seroreversion was strongly associated with sustained maternal viral suppression during pregnancy and preconception ART.
- **The rapid clearance of HIV-1 antibodies in this context highlights the potential for use of non-molecular diagnostic methods earlier in selected settings.**
- These findings warrant validation in larger cohorts before informing changes to diagnostic algorithms.

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