

Mother-to-Child transmission (MTCT) of HIV-2 in the French Perinatal cohort EPF (ANRS CO1/11)

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ABSTRACT

Background: Management of pregnancies with HIV-2 infection remains unclear because of important differences with HIV-1, in terms of natural history and resistance to NNRTIs, and because of its lower prevalence.

Methods: All pregnant women infected by HIV-2 alone, enrolled from 1986 to 2004 in the French Perinatal HIV Cohort, and their children, were eligible for this analysis. Plasma HIV-2 viral load near delivery was quantified with HIV2-RNA real time PCR (cut-off 2.3 log copies/ml) and HIV-2 infection child status was determined using HIV-2 DNA PCR +/-culture and serology after 18 months of age.

Results: Overall, 2.6% (191/7478) mothers enrolled in EPF were HIV-2 infected, most of them born in sub-Saharan Africa (92%). The total number of pregnancies during the study period was 313/9727 (3.2% of the cohort). Among these pregnancies, 94% were in women CDC group A ; CD4 count at delivery was >350/L in 80%, and <200/L in only 7.6%. Antiretroviral therapy (ART) was prescribed in 162 pregnancies (52.6%) : ZDV monotherapy in 69.8%, dual NTRIs in 15.4%, and triple therapy with PI in 14.8%. In most cases, the objective was prevention of MTCT (PMTCT). In 146 pregnancies (47.4%), the mothers received no ART (80.8% of them before 1997), including 4 with CD4< 200/L. Intrapartum ZDV was administered in 53.9% of mothers, and 17.4% of deliveries were elective cesareans; 51.9% of neonates received postnatal prophylaxis with ZDV. In 21.3% of treated mothers with available viral load, HIV2-RNA remained detectable at delivery (median 3.3 log copies/mL). Among the 320 children (including twins), two were HIV-2 infected, a transmission rate of 0.6% (95%CI: 0.08%-2.2%). The first case occurred in 1993, from a mother who had untreated HIV-2 primary infection. The second case occurred in 2002, in a mother inappropriately given a triple therapy with nevirapine; CD4 count was 67 /L and HIV2-RNA 2.9 log copies/mL at delivery.

Conclusion: These findings support current French guidelines for PMTCT, i.e. to use minimal ARV regimen (ZDV) in women with CD4>350/L, and triple ART with PI in women with lower CD4 counts, to reduce the risk of transmission and to treat the mothers HIV-2 disease.

OBJECTIVE

To describe MTCT prevention strategies and to estimate rate of transmission among HIV-2 infected women

PATIENTS AND METHODS

The ANRS French Perinatal Cohort (EPF)

Prospective multicenter national cohort of HIV-infected mother/child pairs
Follow up every 6 months :
→ 2 years old for uninfected children
→ 18 years old for infected children

Study population

- 320 children born to 191 HIV-2 infected mothers between 1985 and 2004
- 9605 children born to 7478 HIV-1 infected mothers
- co-infected HIV-1 / HIV-2 mothers excluded

Variables

- Maternal HIV-2 viral load : HIV2-RNA real time PCR (cut-off 2.3 log cp/ml)
- HIV-2 child diagnostic: using serology at 12-18 months and/or 2 HIV-2 DNA PCR (LTR) after 1 month of age and 3 weeks after the end of postnatal ARV

Table 1 – Prevention of Mother-to-child transmission (MTCT) rate according to maternal HIV type, among last pregnancy (EPF 1985-2004)

	HIV2 (N=191)		HIV1 (N=7287)		p
	n	%	n	%	
HIV diagnosed during pregnancy	81	42.6	2664	36.7	0.09
Late HIV diagnosis(during third gestational trim)	24	12.8	574	8.0	0.02
Late gestational age at booking (≥ 28 weeks)	33	19.1	1162	17.4	0.6
No maternal ARV during pregnancy	79	41.8	1610	22.2	<0.01
Time at starting ARV					
Before or at onset of pregnancy	12	9.9	1716	23.5	<0.01
During pregnancy < 33 weeks	87	71.9	5190	71.1	
During pregnancy ≥ 33 weeks	22	18.2	390	5.4	
Type of last ARV during pregnancy					
Nucleosidic monotherapy	73	66.4	1569	27.9	<0.01
2 NRTI	16	14.6	1461	25.9	
HAART (≥ 3 drugs)	21	19.1	2599	46.2	
Monotherapy among women with CD4<350	11	37.9	543	25.9	0.3
Elective cesarean	41	21.6	2592	35.8	<0.01
Perpartum ARV	111	61.0	5415	78.2	<0.01
Postnatal child ARV	116	61.7	5563	79.1	<0.01
Breastfeeding	4	2.2	43	0.6	0.03

Table 2 – Description of the 2 HIV2- infected children

	INFANT A	INFANT B
• Year of delivery / maternal origin	1993 / Mali	2002 / Mali
• Viral load / CD4 cell count at delivery	<1000 cp/mL / 750 per mm ³	800 cp/mL / 68 per mm ³
• Pre partum / Post partum ARV	no / no	AZT+3TC+efavirenz / AZT
• Mode and gestational age of delivery	vaginal / 38.5 weeks	vaginal / 41 weeks
• Gestational age at delivery	38.5	41
• Breastfeeding	yes until 46 days	yes
• Commentaries	primary infection during pregnancy	inappropriate prepart ART poor treatment adherence possible postnatal transm.
• Siblings	3 younger uninfected children	4 other uninfected children
• % of child CD4 at last evaluation	39% at 5 years old	4% at 5 years old

RESULTS

➤ Characteristics of HIV-2 infected pregnant women

• **Low proportion among mothers-child pairs enrolled in EPF**
2.6% of mothers (191/7478) / 3.2% of pregnancies (313/9727)

• **92% originated from sub-Saharan Africa**
decrease over time in mothers from Africa

• **Older and more often multipara at last pregnancy** (than HIV1)
-> 35 years old: 31% (18.1% in HIV-1)
-> 3 children or more: 42%

• **Rarely symptomatic**
CDC category A : 95 % ; CD4 count at delivery : 5.8% < 200 and 81% ≥ 350/microL

➤ **Less aggressive strategies of MTCT prevention for HIV2 compared to HIV1 infected mothers**
• **42% of HIV2 mothers were not treated during last pregnancy** (versus 22% in HIV1)
• 19% of HIV2 treated mothers received HAART as last ART (versus 46% of HIV1)

➤ **Transmission rate among children born to HIV-2 mother : 0.6% ; 95% CI: 0.08% - 2.2%**
2 infected children among 320 (see description in Table 2)
- Infant A: primary infection during pregnancy
- Infant B: low maternal CD4; possible postnatal transmission: PCR ADN (LTR) negative at 6 mos/positive at 36 months

CONCLUSION

The MTCT rate is very low from HIV-2 infected mothers

PI based HAART is certainly justified for primary infection and advanced disease as indicated in French guidelines for PMTCT:

- triple ART with PI in women with lower CD4 counts or primary infection and to treat the HIV2 disease ; minimal ART regimen (ZDV) in women with CD4 ≥ 350
- discuss cesarean section in case of detectable viral load
- avoid breastfeeding in all cases

Pregnancy is a good opportunity to bring HIV-2 infected women to the health system

Proportion of each sub-Saharan country among HIV-2 mothers included in EPF (%)

