INSERM CESP 1018 - Hôpital de Bicêtre AP-HP 82 rue du Général Leclerc 94276 LE KREMLIN BICETRE Cedex FRANCE

Jeanne Sibiude^{1, 2}, Jérôme Le Chenadec³, Laurent Mandelbrot ^{1, 2}, Alexandre Hoctin³, Catherine Dollfus⁴, Albert Faye^{5,6}, Eida Bui⁴, Emmanuelle Pannier⁷, Jade Ghosn ^{8,2}, Valerie Garrait⁹, Véronique Avettand-Fenoel^{10,11}, Pierre Frange^{10,12}, Josiane Warszawski^{3,13,14}, and Roland Tubiana^{15,16}; for the ANRS-EPF Study Group

1AP-HP Hôpital Louis Mourier, Colombes; ² Université de Paris, IAME UMR 1137, INSERM, Paris; ³INSERM CESP U1018, Le Kremlin-Bicêtre; ⁴AP-HP Hôpital Trousseau, Paris; ⁵AP-HP Hôpital Robert Debré, Paris; ⁶Université de Paris, INSERM, U1123, Paris; ⁷AP-HP, Maternité Port Royal, Paris; ⁸AP-HP. Hôpital Bichat - Claude Bernard, Paris; ⁹Centre Hospitalier inter-communal de Créteil, Créteil; ¹⁰AP-HP Hôpital Necker-Enfants Malades, Paris, France; ¹¹Université de Paris, INSERM U1016, CNRS UMR8104, Institut Cochin, Paris; ¹²EHU 7328 PACT, Institut Imagine, Université de Paris, Paris; ¹³AP-HP Hôpital Bicêtre, Le Kremlin-Bicêtre; ¹⁴Université Paris-Saclay, INSERM CESP U1018, Le Kremlin-Bicêtre, France; ¹⁵APHP, Hôpitaux Université Salpêtrière - Charles Foix, Paris; ¹⁶INSERM, Sorbonne Université, Institut Pierre Louis d'Epidémiologie et de Santé Publique (IPLESP UMRS 1136), Paris; FRANCE.

OBJECTIVE

To estimate the perinatal transmission rate over recent time periods, in the French context of free access to care and absence of breast-feeding, according to timing of ART introduction and viral suppression.

METHODS

The National French Perinatal Cohort (EPF, ANRS CO1/CO11)

Prospective national cohort including all pregnant women with HIV and their children in 90 French centres since 1986, with follow up of all children until 2 years of age.

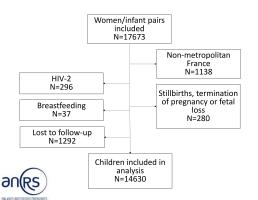
Study population: Inclusion of all HIV-1-infected mothers delivering from 2000 to 2017 and their children. No woman breastfed (Fig1).

Variables: A child was considered infected if HIV-1 DNA and/or RNA PCR results were positive for 2 consecutive samples during the follow-up or if HIV-1 antibodies were detected at ≥18 months of age. A child was considered uninfected if HIV-1 PCR results were negative ≥2 months of age and ≥1 month after ceasing all antiretroviral prophylaxis and/or if results of HIV-1 serology became negative.

Viral suppression was defined for the analysis as viral load < 50 copies/mL, or under the threshold if it was above 50 copies/mL.

Statistical analysis: We compared perinatal transmission (PT) according to time period, timing of ART initiation, maternal plasma viral load (pVL), and gestational age at birth.

Fig 1: Selection of study population. ANRS CO1/CO11.



Among 5482 HIV-infected women treated at conception, virally suppressed at delivery, and not breastfeeding, no case of perinatal transmission was observed:

(0/5482, 95% CI [0-0.07]) virtually eliminating in this group and this context the risk of perinatal transmission.

RESULTS

The proportion of women receiving combined ART increased from 67.7% in 2000-2005 to 97.7% in 2006-2010, and 99.2% in 2011-2017 (p<0.001), as did the proportion receiving ART from conception (28.3%, 46.3% and 65.8%, respectively, p<0.001).

Perinatal transmission rates decreased steadily between the three time periods, from 1.1% in 2000-2005 (58/5,123), 0.7% in 2006-2010 (30/4600), and 0.2% in 2011-2017 (10/4907; p< 0.001). In case of ART initiation before conception, PT rates decreased significantly across time periods, whereas in women not receiving ART at conception, PT rates were similar across time periods (Table 1).

Table 1. HIV-1 perinatal transmission rates according to time period and timing of ART initiation.

| | 2000-2005 N=5067 PT rate | | 2006-2010 N=4441 PT rate | | 2011-2017 N=4738 PT rate | | Р | All time periods N=14246 PT rate | |
|---------------------------|--------------------------------|-------------|--------------------------------|-------------|--------------------------------|------------|-------|--|-------------|
| | | | | | | | | | |
| | | | | | | | | | |
| Timing of ART | % | n/N | % | n/N | % | n/N | | % | n/N |
| initiation | (95% CI) | | (95% CI) | | (95% CI) | | | (95% CI) | |
| Before conception | 0.42 (0.15 - 0.91) | (6 / 1434) | 0.10 (0.01 - 0.35) | (2 / 2055) | 0.03 (0.00 - 0.18) | (1 / 3117) | 0.007 | 0.14 (0.06 - 0.26) | (9 / 6606) |
| 1 st Trimester | 0.31 (0.01 - 1.72) | (1 / 322) | 0.80 (0.17 - 2.32) | (3 / 375) | 0.44 (0.05 - 1.59) | (2 / 452) | 0.68 | 0.52 (0.19 - 1.13) | (6 / 1149) |
| 2 nd Trimester | 1.01 (0.59-1.61) | (17 / 1687) | 0.65 (0.31 - 1.19) | (10 / 1541) | 0.44 (0.12 - 1.11) | (4 / 919) | 0.27 | 0.75 (0.51 - 1.06) | (31 / 4147) |
| 3 rd Trimester | 1.53 (0.97 - 2.29) | (23 / 1503) | 2.55 (1.28 - 4.51) | (11 / 432) | 0.92 (0.11 - 3.29) | (2 / 217) | 0.26 | 1.67 (1.17 - 2.31) | (36 / 2152) |
| Not treated | 9.09 (4.63 - 15.7) | (11 / 121) | 10.53 (2.94 – 24.8) | (4 / 38) | 3.03 (0.08 – 15.8) | (1/33) | 0.52 | 8.33 (4.84 – 13.2) | (16 / 192) |

According to viral suppression

Among 6316 women on ART at conception the proportion virally suppressed at delivery increased steadily over time: 70% in 2000-2005, 89% in 2006-2010, and 93% in 2011-2017 (p<0.001).

No perinatal transmission was diagnosed in 5,482 infants born to women treated at conception and having undetectable viral load near delivery (95%CI [0.00-0.0.7]) (Table 2).

There was no case of PT if the 1st trimester viral load was BLOQ or < 50 copies/mL (0/2358), 95%CI [0-0.16].

Table 2. HIV-1 PT rates among women on ART at conception according to viral load at delivery

| | All time periods | | | | |
|--|---------------------------------------|-----------|--|--|--|
| | N=6316 Perinatal transmission rate | | | | |
| | | | | | |
| Viral load near | % | n/N | | | |
| delivery (cp/mL) | (95% CI) | | | | |
| 4 FO | 0.00 | (0/5247) | | | |
| < 50 | (0.00 - 0.07) | | | | |
| <lower limit="" of<="" td=""><td>0.00</td><td>(0/235)</td></lower> | 0.00 | (0/235) | | | |
| quantification | (0.00 - 1.56) | | | | |
| 50 - 399 | 0.20 | (1 / 504) | | | |
| 30 - 399 | (0.01 - 1.10) | | | | |
| >= 400 | 2.42 | (8 / 330) | | | |
| >= 400 | (1.05 - 4.72) | | | | |

According to gestational age at delivery

PT rate was higher following severe preterm deliveries (<32WG) 2.06%, than in moderate preterm (32WG-36WG) 1.34%, or in term deliveries 0.54% (p<0.001).

However, this association was not found in the period 2011-2017 (0.0 vs 0.19 vs 0.21% respectively), where a higher proportion of women were virally suppressed from the first trimester.

CONCLUSIONS

In the absence of breastfeeding, and in the French context of free access to ART and monthly pVL assessment suppressive ART initiated before pregnancy and continued throughout the pregnancy can eliminate perinatal transmission of HIV.

ACKNOWLEDGEMENTS

Many thanks to all the centers participating in the French Perinatal Cohort, and to the participating mothers and children.

Corresponding author contact information: jeanne.sibiude@aphp.fr