Drift of the Envelope Glycoprotein of HIV-1 Clade B towards Higher Infectious Properties over the Course of the Epidemic

Mélanie Bouvin-Pley, Maxime Beretta, Moreau Alain, Asma Essat, Cécile Goujard, Marie-Laure Chaix, Nathalie Moiré, Loïc Martin, Laurence Meyer, Francis Barin, et al.

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Getting to Zero New Infections: Determinants of HIV Positive Results among Infants Born to HIV Infected Mothers in TASO (U): A Retrospective Review

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Background: In 2012, Uganda revised the EMTCT guidelines to start all pregnant and breastfeeding mothers on ART, this was aimed at virtual elimination of pediatric HIV. We examined the determinants of HIV-positive results among infants born to HIV infected mothers at the 4 TASO centres in Uganda.
Methods: We retrospectively extracted and reviewed data collected in the, EID and post-natal registers at the 4 TASO centres, selected randomly from January 2012 to December, 2015. The HIV 1st PCR test results were used to determine HIV sero status for the infants. We used logistic regression analysis to assess determinants of HIV positive results among infants.
Results: A total of 1736 infants received EID services at the 4 sites and 55 (3.17%) tested positive for HIV, 95% infants received ARVs within 72 hours after birth, whereas 85% of the mothers were already receiving ART under the EMTCT programme. TASO Gulu tested 628 infants, Entebbe 271, Masaka 417 and Mbarara 420. The positivity rate by center was 4.5% for Mbarara, 4.1% for Entebbe, 3.6% for Masaka and 1.6% for Gulu. HIV positive results was significantly associated with parity (AOR=0.696, 95% CI 0.48 1.01, p=0.058), not delivering under skilled labour (AOR=3.90, 95% CI 1.28 11.85, p=0.016), mixed feeding (AOR=3.74, 95% CI 1.36 10.27, p=0.010), infant receiving ARVs beyond 72 hours after birth (AOR=10.8, 95% CI 3.75 31.11, p=0.000) and location of TASO-site Gulu (AOR=0.31, 95% CI 0.09 1.06, p=0.062). HIV status disclosure, ART adherence, marital status, age of the mother, number of ANC visits were not significantly associated with HIV positive results among infants.
Conclusions: We observed low HIV positivity (3.17%) rate below the national EMTCT target of less than 5%, however, the positivity varied across different TASO centres. Mothers practicing mixed feeding, infants receiving ART after 72 hours and not delivering under skilled workers were more likely to transmit the virus to their infants.

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Background: We previously reported evidence that the HIV-1 envelope glycoprotein (Env), especially the gp120, has evolved towards an increasing resistance to neutralizing antibodies at a population level over the course of the epidemic. Here, we investigated whether the antigenic drift of the HIV-1 Env has been associated with modifications of its functional properties, focusing on cell-entry efficacy and interactions with the receptor and co-receptors.
Methods: We compared in cell culture the cell-entry efficacy (infectivity and entry kinetic), the sensitivity to a panel of entry inhibitors (enfuvirtide, CCR5 antagonists and CD4 analogs) and the binding capacity to DC-SIGN, of a panel of Env-pseudotyped viruses derived from patients infected by subtype B viruses at 3 periods of the epidemic (1987-1991, 1996-2000, 2006-2010).
Results: Analyzing the infectivity of our panel of viruses, we found that viruses from patients infected during the most recent period were approximately ten fold more infectious than viruses from patients infected at the beginning of the epidemic. This increase in infectivity was associated with an increase of the viral entry kinetic, the contemporary viruses entering the target cells approximately twice faster than historical viruses. Contemporary viruses were also twice more resistant to the fusion inhibitor enfuvirtide than historical viruses. Interestingly, the higher resistance to enfuvirtide correlated with a higher resistance to CCR5 antagonists, suggesting that contemporary viruses expanded their CCR5 usage efficiency. Viruses were equally captured by DC-SIGN but after binding to DC-SIGN, contemporary viruses infected target cells more efficiently than historical viruses.
Conclusions: Together, our results provide evidence for improved infectious properties of HIV-1 Env during the course of the epidemic, which could impact the viral fitness during the transmission process and might have contributed to the potential increasing virulence of HIV-1.

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