Immune status and uptake of antiretroviral interventions to prevent mother-to-child transmission of HIV-1 in Africa.

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Pregnancy, immune status and uptake of antiretroviral interventions to prevent mother-to-child transmission of HIV-1 in Africa

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Abstract

The aim of this study was to describe the distribution of CD4+ T cell count (CD4) of HIV-1 infected pregnant women diagnosed during prenatal counseling and testing (VCT), in Abidjan, Côte d'Ivoire, and to assess whether HIV-related immunodeficiency influenced or not the acceptance of an antiretroviral package to prevent mother-to-child transmission. Between April and June 2002, CD4 count was systematically performed in all women diagnosed as HIV-infected (n=221) in five antenatal clinics carrying out VCT. Their median CD4 was 408 cells/mm^3 and 14% were < 200 CD4. The overall uptake of the intervention (31.9%) was independent of the immune status.

Keys words: HIV, MTCT, Africa, prenatal counselling and testing, antiretroviral

Introduction

Maternal CD4+ T cell count (CD4) is strongly associated with HIV disease progression and is a strong predictor of mother-to-child transmission of HIV-1 (MTCT) and its prevention (PMTCT) with antiretrovirals [1, 2].Yet, given the low uptake of PMTCT interventions in African settings, generally around 20% [1, 3], the CD4 distribution among the overall population of HIV-infected pregnant women is still unknown. Our hypothesis in Abidjan, Côte d'Ivoire, was that women less advanced in HIV disease felt no interest in receiving PMTCT interventions and self-excluded themselves during antenatal follow-up. The stigmatization towards HIV-infected patients and the inappropriate attitude of some health workers described in this population could lead to this self-exclusion [4, 5]. The aim of this study was to describe the CD4 distribution in all women diagnosed antenatally as HIV-infected and to study the relation between immune status and the uptake of a PMTCT antiretroviral-based intervention.

Population and methods

Since March 2001, the Ditrame Plus ANRS 1201/1202 project has provided a comprehensive PMTCT package (perinatal antiretroviral intervention and proposition of alternatives to prolonged and predominant breastfeeding) in seven antenatal clinics in Abidjan, Côte d'Ivoire [6, 7]. In April 2002, a CD4 prevalence survey was conducted within this project. After individual pre-test counseling, HIV testing was systematically proposed as before to every pregnant women attending these antenatal clinics. After having accepted HIV testing and signed an informed consent document, pregnant women were enrolled in the prevalence survey. Two venous blood samples were collected. The first sample was used for the diagnosis on-site of HIV-1 infection using rapid HIV testing (Determine™ and Genie2™). HIV test result was made available within 24 hours after blood collection. Women were considered as HIV-1 infected (HIV+) if both tests were positive. The second sample was shipped to a reference laboratory (CeDReS, Treichville University Hospital, Abidjan) to perform the CD4+ count in all HIV+ women by standard flow cytometry

[FACScan Becton Dickinson]. All HIV+ pregnant women were followed until delivery to determine the proportion who received their HIV test result during an individual post-test counseling and among them, those who started the prophylactic antiretroviral regimen.

Results

Between April and June 2002, 2407 pregnant women received a prenatal counseling and 2144 (89.1%) accepted HIV testing. The women who refused to be tested were comparable to those who accepted in terms of parity and gestational age, but were older by 14 months on average (27.0 ± 5.3 vs 25.8 ± 5.6 years; p<0.001). The prevalence of HIV-1 infection was 10.5% (n=226; 95% confidence interval [9.2%-11.9%]). A total of 172/226 HIV+ women (76.1%) returned to the clinics to receive their HIV test result, a proportion comparable to the return rate of HIV-uninfected women (76.9%).

All but five HIV+ pregnant women diagnosed antenatally had a CD4 count measurement. Overall, their median CD4 count was 408 cells/mm^3, Interquartile Range (IQR) [304–570] (Table 1). No difference in CD4 count was found between the 50 (22.6%) HIV+ women who did not receive their HIV test result and the 171 who received it, i.e. the 99 informed of their sero-status but who did not initiate PMTCT and the 72 informed and initiating antiretroviral prophylaxis (389 vs 420 cells/mm^3 in median; p=**???**). Considering individual expected dates of delivery as the censoring time, 72/226 women (31.9%) received the PMTCT antiretroviral regimen. There was no difference in CD4 count between HIV+ women who started it and those 149 who did not (405 vs. 420 in median ; p= **???**).

Discussion and conclusion

To our knowledge, this study is the first to describe the immune status of all HIV+ women diagnosed antenatally in an African setting of high HIV-1 prevalence in relation to their uptake of a PMTCT intervention. The CD4 count was similar in HIV+ women who did not return for their test result and those who were informed their sero-status. No difference was also found in HIV+

infected pregnant women who did not accept the PMTCT antiretroviral prophylaxis and those who received the PMTCT package. Thus, in our study, the low uptake of the Ditrame Plus program cannot be explained by the self-exclusion of pregnant women in relation with advanced HIV disease. We did not use any clinical criteria such as the AIDS stage to perform these comparisons as it would grossly underestimate the proportion of women with advanced HIV disease. However, in our population stigma could well be the main factor limiting the uptake of the PMTCT program. Population-specific research must be required to understand the different factors influencing the low uptake of the PMTCT interventions in sub-Saharan Africa. CD4 prevalence surveys might be helpful to adjust PMTCT antiretroviral strategies to women needs [1].

References

1. Dabis F, Ekpini ER. HIV-1/AIDS and maternal and child health in Africa. *Lancet.* Jun 15 2002;359(9323):2097-2104.
2. Leroy V, Karon JM, Alioum A, et al. Twenty-four month efficacy of a maternal short-course zidovudine regimen to prevent mother-to-child transmission of HIV-1 in West Africa. *AIDS.* Mar 8 2002;16(4):631-641.
3. Cartoux M, Meda N, Van de Perre P, Newell ML, de Vincenzi I, Dabis F. Acceptability of voluntary HIV testing by pregnant women in developing countries: an international survey. Ghent International Working Group on Mother-to-Child Transmission of HIV. *AIDS.* Dec 24 1998;12(18):2489-2493.
4. Méda N, Leroy V, Viho I, et al. Acceptability and field efficacy of a routine utilisation of zidovudine to reduce mother-to-child transmission of HIV-1 in West Africa. *AIDS.* 2002;16(17):2323-2328.
5. Horo A, Bequet L, Viho I, et al. Knowledge and attitudes about HIV infection amongst health professionals working in prevention of mother-to-child transmission of HIV. Abidjan,

Cote d'Ivoire. [10BT5-2]. Paper presented at: XIIth International Conference on AIDS and STDs in Africa, 2001; Ougadougou, Burkina-Faso.

6. Dabis F, Ekouevi D, Bequet L, et al. A Short Course of Zidovudine + Peripartum Nevirapine is Highly Efficacious in Preventing Mother-to-Child Transmission of HIV-1: The ANRS 1201 DITRAME-plus Study, Abidjan, Côte d'Ivoire. Poster N°854. Paper presented at: The 10th Conference on Retroviruses and Opportunistic Infections, 2003; Boston, USA.

7. Leroy V, Bequet L, Ekouevi D. Uptake of infant feeding interventions to reduce postnatal transmission of HIV-1 in Abidjan, Cote d'Ivoire. The DITRAME PLUS ANRS 1202 project [MoPeD3677]. Paper presented at: XIV international AIDS conference, 2002; Barcelona, Spain.

Table 1 : CD4+ T Lymphocyte count (CD4) distribution in HIV-1 infected pregnant women diagnosed in five antenatal clinics during voluntary counseling and testing in Abidjan, Côte d'Ivoire, ANRS 1201/1202 Ditrame Plus Project, April-June 2002.

	TOTAL (N=226)	**Did not receive ARVs for PMTCT (n=154)**		**Received ARVs for PMTCT (n=72)**	**P ***	**P ****
		Did not receive test result (n=54)	**Received test result (n=100)**			
CD4 measurement (n)	221	50 [A]	99 [B]	72 [C]		
Absolute CD4 count						
Mean ± SD	452.5 ± 251.7	433.9 ± 326.2	466.7 ± 223.0	445.8 ± 231.5		
Median [IQR]	408 [304 – 570]	389 [262 – 515]	425 [313 – 616]	405 [308 – 516]		
CD4 distribution:						
< 200/mm^3	31 (14.0)	10 (20.0)	11 (11.1)	10 (14.5)		
200 – 349/mm^3	47 (21.3)	12 (24.0)	22 (22.2)	13 (18.1)		
350 - 499/mm^3	66 (29.9)	12 (24.0)	28 (28.3)	24 (34.8)		
>=500/mm^3	77 (34.8)	16 (32.0)	38 (38.4)	22 (31.9)		
Percentage of CD4						
Mean ± SD	26. 2 ± 10.3	25.1 ± 10.7	26.6 ± 10.5	26.4 ± 9.6		
Median [IQR]	26.6 [19.5–32.0]	25.1 [19.3–30.5]	27.0 [20.0–32.7]	27.3 [19.6–31.8]		
< 15%						

IQR: Interquartile range, SD: Standard deviation, DP: Ditrame Plus Project, ARVs: antiretroviral prophylaxis regimen (Zidovudine + Nevirapine), PMTCT: prevention of mother to child transmission of HIV.

* : A vs. B+C

** : A+B vs. C