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Continuous free access to HAART could be one of the potential factors impacting on loss to follow-up in HAART-eligible patients living in a resource-limited setting: N'djamena, Chad

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Background: Retention of HAART-eligible HIV-infected patients in clinical follow-up systems are now becoming an important issue in sub-Saharan African countries.

Methods: In this retrospective study (April 2008 to November 2011), we assessed the attrition rate variations in a cohort of 509 HAART-eligible patients in Chad.

Results: Decrease in levels of loss to follow-up were observed during the implementation of continuous free access to HAART (72.5 vs. 10%; $p < 0.001$) and was independent of gender, age, WHO clinical stage and CD4+ T cell count at inclusion and of the time delay to initiate HAART ($p > 0.48$).

Conclusions: These data suggest that the implementation of free access to HAART without any interruption of supply, from autumn 2009, could be the factor that potentially changed the HIV patient attrition rate in this resource-limited setting.

Keywords: Chad, HAART, HIV, Loss to follow-up, Sub-Saharan Africa

Introduction

Sub-Saharan Africa still bears the heaviest burden of the HIV pandemic despite recent decreasing trends in HIV prevalence, during 2000–2009, due to better access to highly active anti-retroviral therapy (HAART).^{1,2} However, only patients who have been actively followed-up can positively benefit from HAART.² Because HAART-treated patients lost to follow-up are assumed to rapidly select HAART-resistant HIV strains and to develop fatal opportunistic infections in the following months, retention of HIV-infected patients is now becoming an important issue in sub-Saharan African countries.^{3–6} There are only a few published epidemiological reports from Chad, with no data available since the implementation of free access to HAART in N'djamena.⁷ Chad is one of the poorest countries in the world with a national growth index per capita of US\$690. HIV prevalence is estimated at 3.1% of the Chadian adult population, with great discrepancies between regions, ranging from 8.1% in N'Djamena to 10% in southern areas.⁷ Continuous free access to HAART has been in effect since 2008, but with infrequent supply, and was only

considered as continuous in N'djamena since October 2009.⁸ We conducted a retrospective cohort study to explore the impact of implementation of continuous free access to HAART on patient loss to follow-up in N'djamena, Chad.

Methods

Hospital background

In the capital city of Chad, N'Djamena, secondary and tertiary healthcare consists mainly of three hospitals: Hôpital Général de Référence Nationale, Hôpital de la Liberté and Hôpital 'Le Bon Samaritain', which is located in an impoverished area housing approximately 450 000 residents. Our study was conducted from April 2008 to November 2011 in Le Bon Samaritain. The hospital consisted of 147 beds in a secondary healthcare centre and was officially inaugurated at the end of 2007. Funding sources for this hospital originate from the Chadian state, French association 'Haut de Seine' and Jesuits' congregations.

HIV consultation and delivery of antiretroviral drugs for adult patients

Daily, HIV-infected patients attending the HIV external consultation at Bon Samaritain teaching Hospital in N'djamena were examined by senior medical doctors. At the end of the medical consultation these patients were referred to hospital's pharmacy where they were provided with antiretroviral drugs (ARVs) for a month-long treatment. The Chadian pharmaceutical central purchasing body (CPCPB) stocked all the ARVs in the hospital's pharmacy and also provided ARVs in N'djamena city and surrounding areas.

A local pharmacist continuously managed a 4-month stock of ARVs for the 600 HAART-eligible HIV-infected patients at the Bon Samaritain hospital. The pharmacist performed an inventory twice a month and would alert the CPCPB if there was a shortage of stock (<1 month's supply). The stock would be replenished within 48 hours. Each month, the pharmacist provided the physicians with an inventory report of the ARV drug stocks.

If consulting patients were unable to get the prescribed ARVs, patients were immediately sent back to the physicians to get another ARV prescription of drugs that were available. Using this system, physicians were immediately made aware of when stock had run out. The same procedure was used prior to and after 2009.

No specific interventions known to have an impact on the attrition rates, like community-based accompaniment for medical follow-up or antiretroviral therapy delivery, had been performed during this study period. Peripheral blood CD4+ T lymphocyte counts were determined at the Hôpital Général de Référence Nationale, using FACS® count (Becton Dickinson, Rungis; France) according to manufacturer's instructions. Since October 2010, patient's medical records were created and stored at the hospital Le Bon Samaritain.

Financial background

In 2007, the Chadian government announced free access to HAART for HIV-infected patients. However, during 2007–2008, when HAART was only financed by the Chadian State, the free access was not available to all. Patients had to pay approximately 15 000 CFA franc for first line of HAART regimens (US\$30.67) and stock shortages were numerous (3–6 times a year) in the CPCPB. Since 2009, HAART was financed by the Chadian State, as well as the Global Fund to fight against AIDS, Tuberculosis and Malaria. From October 2009 to November 2010, free access to HAART was fully effective, without stock shortages in the peripheral hospital (Le Bon Samaritain) (O. Djarma; personal communication). All of the demographic, clinical, virological and immunological data obtained from patients included in the study, during this free continuous access to ARVs time-period, were compared with those obtained from patients included between April 2008 to November 2009, when access to ARVs were not free or continuous.

Inclusion criteria of the study patients

All of the HIV-positive adult patients eligible for HAART (defined as WHO clinical stage 3 or 4,⁹ or CD4+ T lymphocyte count <250 cells/mm³ irrespective of WHO staging), and attending the HIV

external consultation at Bon Samaritain teaching hospital in N'djamena were included in the present study. Demographic, clinical, virological and immunological data were retrospectively extracted from the hospital register (until October 2010), and then data were taken from each patient's medical record. Information captured included: age, place of residence, clinical and immunological data at the time of inclusion (WHO clinical stage peripheral blood CD4+ T-lymphocyte counts), time of HAART delivery and time delay between the HIV serological diagnosis and the initiation of HAART. Upon inclusion, patients visited the HIV clinic every month for clinical exams and received direct HAART delivery from the pharmacist.

Loss to follow-up was defined as a time delay of >3 months since the last scheduled visit. At the end-point of the present retrospective study (3 months later after the last inclusions in November 2011), clinical outcomes were sought for each included patient (active clinical follow-up, loss to follow-up, transferred to another facility or dead).

Statistical analyses

Using Stat view 5.0 software (SAS institute Inc., Carv, NC, USA); quantitative variables were compared using the Mann Whitney U-test and qualitative variables were compared using Pearson's χ^2 test. P-values of <0.05 were considered as significant.

Results

Among the 509 included adult patients (median age=32 [15–76] years), 302 (59.3%; 302/509) were female and 418 (82.1%; 418/509) were living in N'Djamena city. At the time of inclusion, a WHO clinical stage superior or equal to 3 was found in 47.9% (244/509) of the 509 study patients. HAART was delivered in 484 (95.0%; 484/509) of the 509 study HIV-infected patients and in 91% of patients, consisted of two nucleoside reverse transcriptase inhibitors associated with a non-nucleoside reverse transcriptase inhibitor (first line of HAART regimen in Chad). Median CD4+ T lymphocytes counts were 182 cells/mm³ (5–399) at the time of inclusion. At the end-point of the present retrospective study, 284 (55.8%; 284/509) of the 509 selected patients were still being actively followed-up, 182 (35.8%; 182/509) were lost to follow-up, 24 (4.7%; 24/509) had died and 19 (3.7%; 19/509) had been transferred to another facility. A yearly-stratified analysis of the included patients was performed and summarized in Figure 1, displaying the distribution of the total number of patients according to their end-point cohort status, as well the cumulative number of patients actively followed-up between 2008 and 2011. Interestingly, we observed that between April 2008 and October 2009, 152 of 210 (72.3%) HAART-eligible patients were lost to follow-up during the discontinuous or 'not free' access period to HAART, whereas during implementation of continuous free access to HAART (October 2009 to November 2011), levels of loss to follow-up were 10% (30/299) among the HAART-eligible patients (72.3 vs 10%; $p<0.001$). Table 1 shows the flow chart that enabled us to generate Figure 1. It should be noted that that among these yearly stratified results, patients lost to follow-up during the year of inclusion were not re-included in the cohort. However, patients that were actively followed-up, were not lost during the following years. These results may reflect the 'real-life' situation in central Africa that HIV infectious diseases specialist

face. Another way to explain our hypothesis was that levels of loss to follow-up were lower in the continuous free access to HAART period than the previous discontinuous access to HAART period. If we assumed that loss to follow-up was a linear phenomenon, and that patients lost to follow-up were distributed along the observed period for each cohort, then we could speculate a 4-year loss to follow-up proportion as: 1. 2008: only 16 out of 85 patients (90 minus 3 patients transferred to another facility minus 2 deceased patients) were followed-up for 4 years (real-life data); 2. 2009: only 28 out of 111 patients were followed-up for 3 years, corresponding to annual decrease of 24.9%. The

expected number of patients actively followed-up at 4 years would be 21; 3. 2010: 87 out of the 111 patients were followed-up for 2 years corresponding to an annual decrease of 10.9%. The expected number of patients actively followed-up at 4 years would be 69; 4. 2011: 153 out of 159 patients were followed-up for 1 year, corresponding to an annual decrease of 3.8%. The expected number of patients actively followed-up at 4 years would be 136.

Thus, in the 2008–2009 cohort, the total number of patients actively followed-up would be 21+16=37, corresponding to an estimated percentage of 37/196=18.8%. In the 2010–2011 cohort, the total number of patients actively followed-up would be 69+136=205, corresponding to an estimated percentage of 205/270=75.9%. We could not assume that these two cohorts are identical because the χ^2 Pearson test between these two proportions was $p < 10^{-4}$, indicating that the annual decrease of patients was not similar between the two time periods. This statistically significant result means that: 1. there would be a greater number of patients actively followed-up in the 2010–2011 cohort, even in the worst hypothesis that assumed that loss to follow-up was a linear phenomenon, and which increased a 4-year loss-to-follow-up proportion in the 2010–2011 cohort more than in the 2008–2009 cohort; 2. in real-life (where the loss to follow-up phenomenon was probably, according to our experience, not linear), results for the 2010–2011 cohort would be better than those estimated here as statistically significant.

These attrition rate variations appeared to not be associated with gender, age, WHO clinical stage and CD4+ T cell counts at inclusion, as well as with the time delay to initiate HAART ($p > 0.48$). Patients lost to follow-up were more frequently living outside N'Djamena than those actively followed-up (24.2% vs 9.2%; $p = 0.001$). These data suggest that the implementation of free access to HAART, without any lack of supply, from autumn 2009 could be the factor that potentially changed the HIV-patient attrition rate.

Discussion

In this present retrospective study performed in a district hospital located in southern N'Djamena, Chad, a statistically significant decrease in the levels of HIV-infected patients lost to follow-up was observed post-October 2009 (Figure 1). No known interventions, like community-based accompaniment for medical follow-up or antiretroviral therapy delivery that could have had an impact on attrition rates were initiated, increased or stopped

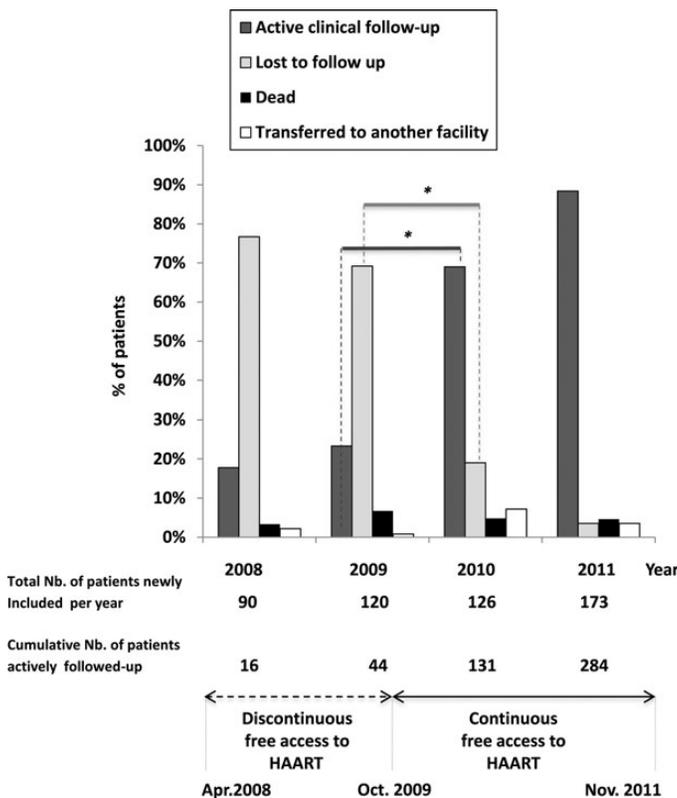


Figure 1. Yearly-stratified analysis of the included patients according to their end-point cohort status during the study period (April 2008 to November 2011) in a district hospital of N'djamena, Chad. * p-values <0.001.

Table 1. Summary of patients lost to follow-up in the Bon Samaritain teaching hospital, N'Djamena, Chad between April 2008 and November 2011

Year	Patients included during year	Deceased patients	Patients transferred to another facility	Patients lost to follow-up during the year	Patients actively followed-up to November 2011
2008 (April to December)	90	2	3	69	16
2009	120	8	1	83	28
2010	126	6	9	24	87
2011 (until November)	173	8	6	6	153

during the study period.¹⁰ The implementation of free access to HAART (without any supply interruptions) from autumn 2009, was retrospectively suspected to be the unique event that affected HIV-patient attrition rates. In the present study, the increased retention rate observed after the period of continuous free access to HAART was not influenced by age, gender, WHO clinical stage and by the CD4+ T-lymphocyte counts recovered at the time of inclusion. Taken together, our findings indicate that continuous free access to HAART could be an independent factor that might have had a significant impact on the loss to follow-up in this resource-limited setting. This hypothesis is indirectly supported by a recent study that reported high attrition rates in HAART-untreated WHO stages 1 and 2 patients in a rural hospital setting in Malawi.⁴ Similarly, a clinical study concluded that South Africa's 2011 expansion of the HAART guidelines could be enacted without increasing program attrition.¹¹ However, our retrospective study had some limitations. The HIV-infected population lost to follow-up was 'per se' inaccessible to further investigations as our investigation was not a prospective time series analysis, but a preliminary retrospective study. Therefore, direct or indirect factors explaining why HAART eligible patients were lost to follow-up before and after implementation of continuous free access to HAART remains undefined in the present study. Further prospective multi-centric clinical investigations in Africa are needed to confirm our present data suggesting that continuous free access to HAART could result in reduced loss to follow-up in a resource-limited setting.

Conclusions

Our retrospective cohort study suggested that continuous free access to HAART could be one of the potential factors increasing the retention rate of HIV-infected patients in a resource-limited setting.

Authors' contributions: OD and LA conceived the study; OD, LA and YN designed the study protocol; OD and LA carried out the clinical assessment; YN and FR analyzed and interpreted the data; YN, FB and LA drafted the manuscript; OD, AD and FR critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. OD and LA are guarantors of the paper.

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Competing interests: None declared.

Ethical approval: Not required.

References

- 1 Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS World AIDS Day report, 2011. Geneva: United Nations; 2011. http://www.unaids.org/en/media/unaids/contentassets/documents/unaids_publication/2011/jc2216_worldaidsday_report_2011_en.pdf [accessed 13 June 2014].
- 2 Joint United Nations Programme on HIV/AIDS (UNAIDS). Global HIV/AIDS Response. Epidemic update and health sector progress towards Universal Access. Geneva: United Nations; 2011. http://www.who.int/hiv/pub/progress_report2011/ [accessed 13 June 2014].
- 3 Fox MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007–2009: systematic review. *Trop Med Int Health* 2010;15(Supp 1):1–15.
- 4 Tayler-Smith K, Zachariah R, Massaquoi M et al. Unacceptable attrition among WHO stages 1 and 2 patients in a hospital-based setting in rural Malawi: can we retain such patients within the general health system? *Trans R Soc Trop Med Hyg* 2010;104:313–9.
- 5 Brinkhof M, Pujades-Rodriguez M, Egger M. Mortality of patients lost to follow-up in antiretroviral treatment programmes in resource-limited settings: systematic review and meta-analysis. *PLoS One* 2009;4:e5790.
- 6 Koyalta D, Charpentier C, Beassamda J et al. High frequency of antiretroviral drug resistance among HIV-infected adults receiving first-line highly active antiretroviral therapy in N'Djamena, Chad. *Clin Infect Dis* 2009;49:155–9.
- 7 UNICEF. Chad statistics. New York, USA: UNICEF; 2011. <http://www.unicef.org/infobycountry/> [accessed 13 June 2014].
- 8 United Nations Office for the Coordination of Humanitarian Affairs. AIDS in Chad the neglected crisis. Geneva: United Nations; 2008. <http://www.irinnews.org/pdf/in-depth/plusnews-aids-in-chad-the-neglected-crisis-june-2008.pdf> [accessed 13 June 2014].
- 9 WHO. Revised World Health Organization Clinical Staging of HIV/AIDS for Adults and Adolescents. Geneva: World Health Organization; 2005. <http://www.who.int/hiv/pub/guidelines/en/> [accessed 13 June 2014].
- 10 Franke MF, Kaigamba F, Soggi AR et al. Improved retention associated with community-based accompaniment for antiretroviral therapy delivery in rural Rwanda. *Clin Infect Dis* 2013;56:1319–26.
- 11 Clouse K, Pettifor A, Mhairi M et al. Initiating antiretroviral therapy when presenting with higher CD4 cell counts results in reduced loss to follow-up in a resource-limited setting. *AIDS* 2013;27:645–50.