Incidence and Risk Factors for Follow-Up Interruption of HIV-Infected Patients in Guadeloupe

Narcisse Elenga, Marie-Thérèse Georger-Sow, Thierry Messiaen, Isabelle Lamaurie, Isabelle Favre, Mathieu Nacher, Gilles Beaucaire

To cite this version:

HAL Id: inserm-00915235
https://www.hal.inserm.fr/inserm-00915235
Submitted on 6 Dec 2013

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
Incidence and Risk Factors for Follow-Up Interruption of HIV-Infected Patients in Guadeloupe

Narcisse Elenga¹, Marie-Thérèse Georger-Sow², Thierry Messiaen³, Isabelle Lamaurie¹, Isabelle Favre², Mathieu Nacher¹,⁴ and Gilles Beaucaré³

¹Service de Pédiatrie, Centre hospitalier de Cayenne « Andrée Rosemon », Rue des Flamboyants, BP 6006-97306 Cayenne cedex, Guyane Française
²Coordination Régionale VIH (COREVIH) Guadeloupe CHU de Pointe-à-Pitre/Abymes Bâtiment B Ancien hôpital Ricou 2ème étage BP 465 97159 Pointe-à-Pitre Cedex, Guyane Française
³Service des maladies infectieuses, Guadeloupe CHU de Pointe-à-Pitre/Abymes Bâtiment B Ancien hôpital Ricou 2ème étage BP 465 97159 Pointe-à-Pitre Cedex, Guyane Française
⁴Coordination Régionale VIH (COREVIH) Centre hospitalier de Cayenne « Andrée Rosemon », Centre d’Investigation Clinique Épidémiologie Clinique CIC EC Antilles Guyane CIE 802, Guyane Française

Abstract

Background: Guadeloupe is the region of France with the second highest prevalence of HIV.

Methods: To determine the risk factors for being lost to follow-up (LFU), a retrospective cohort study of 2,732 patients followed between 1988 and 2009 was conducted, and determined which variables were related to being LFU, i.e. permanently disappearing from HIV clinics or coming back after more than one year of missed appointments.

Results: The incidence rate for permanent follow-up interruption was 9 per 100 person-years (8.3-9.7 person-years). The median time of LFU was 6.4 years (interquartile range 3.1-16.9 years). Cox modelling showed that the younger age groups (HR: 1.60[1.30-2.10], p=0.000) and patients diagnosed before 1997 (HR: 4.80[3.60-6.50], p=0.000) were significantly more likely to be permanently LFU. However, patients treated with HAART had a lower risk of being LFU (HR: 0.63[0.51-0.80], p=0.000).

Conclusion: These results suggest that some patients may have died. They also allow to quantify the magnitude of a major yet often under-recognized problem and to identify its predictors in the context of Guadeloupe. This could help clinicians improve patient retention.

Keywords: HIV-infected patients; Follow-up interruption; Risk factors; Guadeloupe

Abbreviations: HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome; LFU: Lost to Follow-Up; HR: Hazard Ratio; HAART: Highly Active Antiretroviral Therapy; GFHDH: Guadeloupe Section of the French Hospital Database for HIV; GHDH: Guadeloupean Hospital Database on HIV infection; CISH: Centre d’Information et de Soins de l’Immunodéficience Humaine ; RNA: Ribonucleic Acid; INSERM: Institut National de la Recherche Médicale; CNIL: Commission Nationale Informatique et Libertés; CDC: Centers for Disease Control and Prevention; IQR: Interquartile Range

Introduction

Guadeloupe is part of the French overseas territories, and has a large number of persons living with HIV/AIDS. Transmission is mostly heterosexual, and the proportion of infected women is high, i.e. almost half of all those infected. Moreover, in Guadeloupe, a large proportion of patients are foreigners (mainly from Haiti) [1,2]. The standards of healthcare in Guadeloupe are similar to those of metropolitan France. All patients infected with human immunodeficiency virus (HIV) may receive free antiretroviral treatment (including the most recent drugs) regardless of their nationality or their socio-economic level. Radiology, viral loads, CD4 counts and HIV genotyping, as well as antiretroviral drug monitoring are available for routine care. Since 1996, the use of highly active antiretroviral therapy (HAART) in developed countries has led to a decrease in the morbidity and mortality of patients infected with HIV [3,4]. However, despite the availability of more effective treatments for HIV infection, some patients under care stop their clinical follow-up. These patients are at major risk of developing AIDS-defining illnesses leading to death. A recent analysis of data from the Guadeloupe section of the French Hospital Database for HIV (GFHDH) suggested a persistently high proportion of late presenters for HIV diagnosis and HIV care in Guadeloupe [5]. The follow-up of patients is of paramount importance to measure their immunovirological status and eventually start or optimize anti-retroviral therapy, and to screen for and prevent HIV-related morbidity and mortality. In Guadeloupe, no data have been reported regarding patients who are lost to follow-up. This study aimed to describe predictors of loss to follow-up (LFU) in the Guadeloupean Hospital Database on HIV infection (GHDH).

Materials and Methods

Description of the FHDH

GHDH is part of the French Hospital Database on HIV. The characteristics of the FHDH have been described in detail elsewhere [6]. Briefly, FHDH is a clinical epidemiological network implemented, since 1992, in 62 French University Hospitals belonging to 29 HIV treatment and information centres (CISH) located both in continental France and overseas territories. The only FHDH inclusion criteria are

*Corresponding author: Narcisse Elenga, Service de Pédiatrie, Centre hospitalier de Cayenne, Andrée Rosemon, Rue des Flamboyants, BP 6006-97306 Cayenne cedex, Guyane Française, Tél: +595 694 978 048 ; Fax: +594 594 394 819; E-mail: elengafl@yahoo.fr

Received July 30, 2013; Accepted August 28, 2013; Published September 03, 2013


Copyright: © 2013 Elenga N, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
documented HIV-1 or HIV-2 infection and written informed consent. Data are recorded prospectively by trained research assistants, using DMI2 software (property of the French Ministry of Health). The standardised data collection form includes baseline characteristics, the usual biologic markers such as CD4 cell counts and plasma HIV-RNA levels, clinical manifestations, treatments, clinical trials in which the patients are enrolled, death, and the cause of death, as reported in the medical records.

Patients
The HIV-positive patients followed in Guadeloupe since 1 January 1988 and at St. Martin Hospital since 1 January 1992 until 31 December 2009 were enrolled in the GFHDH. Time-dependent variables such as sex, nationality, and contamination mode and time-dependent variables such as age, CD4 counts, HIV1 viral loads, treatments, and clinical events are routinely entered by trained clinical studies technicians. Patients included in the FHDH gave informed consent for the use of their data. Their identity was encrypted before the data were sent to the Ministry of Health and the Institute National de la Recherche Médicale (INSERM), which centralises data from the Centres for Information and Care of HIV (CISH) throughout France. This data collection was approved by the Commission Nationale Informatique et Libertés (CNIL), a national committee that oversees research data.

Definition of patients lost to follow-up (LFU)
Patients were considered permanently LFU if they had permanently disappeared from HIV clinics, excluding patients known to be deceased. Temporary interruption of follow-up was defined as a period of more than 1 year before consulting again [7].

Variables
Age was divided into three groups: <30 years, 30-40 years, and >40 years. The other explanatory variables were gender, drug addiction (alcohol, marijuana smoking, crack or cocaine use), HIV diagnosis period, CD4 count at enrolment (categorised as <200, 200-499, and ≥ 500 cells/mL), CDC categories A, B, and C, ART initiation period, and history of psychiatric problems during follow-up. We created three categories for period of inclusion: 1988-1996, 1997-2004 and 2005-2008.

Statistical analysis
The factors associated with LFU were analysed by Cox models yielding adjusted hazard ratios (HR). For all tests performed, a p-value of 0.05 or less was considered as statistically significant. The data were analysed with STATA 10.0 (Stata Corp LP, College Station, TX, USA). The proportionality of the hazard functions was determined graphically using Schoenfeld residuals. A total of 2732 subjects with 46722 person-years of follow-up.

Table 1 shows that patients in the younger age group and patients diagnosed before 1997 were most likely to be LFU while patients treated with HAART had a low risk of being LFU. Table 2 globally shows the similar risk factors than Table 1.

Table 1: Risk factors for permanent follow-up interruption of HIV-infected patients in Guadeloupe.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Incidence rate (/100 person-years)</th>
<th>Hazard ratio* (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>14</td>
<td>1.6 (1.30-2.10)</td>
<td>0.000</td>
</tr>
<tr>
<td>30-40</td>
<td>8.6</td>
<td>1.30 (1.10-1.60)</td>
<td>0.012</td>
</tr>
<tr>
<td>&gt;40</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>1.10 (0.90-1.30)</td>
<td>0.5</td>
</tr>
<tr>
<td>HIV diagnosis period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005-2008</td>
<td>2.5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1997-2004</td>
<td>7</td>
<td>3.10 (2.28-4.23)</td>
<td>0.000</td>
</tr>
<tr>
<td>1988-1996</td>
<td>14</td>
<td>4.3 (3.50-6.50)</td>
<td>0.000</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial CD4&lt;200/mm³</td>
<td>3</td>
<td>0.47 (0.34-0.65)</td>
<td>0.000</td>
</tr>
<tr>
<td>Initial CD4&lt;200-499/mm³</td>
<td>7.3</td>
<td>0.82 (0.68-0.98)</td>
<td>0.032</td>
</tr>
<tr>
<td>Initial CD4≥500/mm³</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>CDC categories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>6</td>
<td>0.70 (0.53-0.85)</td>
<td>0.001</td>
</tr>
<tr>
<td>C</td>
<td>2.7</td>
<td>0.38 (0.28-0.53)</td>
<td>0.000</td>
</tr>
<tr>
<td>Known drug use/addiction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>8</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>10</td>
<td>0.7 (0.31-1.50)</td>
<td>0.4</td>
</tr>
<tr>
<td>ARV therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAART+</td>
<td>4</td>
<td>0.63 (0.51-0.80)</td>
<td>0.000</td>
</tr>
<tr>
<td>HAART-</td>
<td>12</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*Obtained using a Cox proportional hazard model including all the above mentioned covariates.
CI: confidence interval; py: person-years

Discussion
More than 22% of the patients from our cohort were permanently LFU. This proportion is high but it is lower than in French Guiana where a third of the cohort was permanently lost to follow up. This study shows some of the factors underlying this high rate of loss to follow-up in Guadeloupe. Younger patients, earlier year of HIV diagnosis, patients not receiving any treatment, and patients diagnosed with a moderate CDC stage were more likely to disappear. This confirms other studies performed in HIV patients [8]. Guadeloupe, like French Guiana, takes in large numbers of clandestine immigrants from neighbouring countries. Irregular immigrants may try to avoid all contact with the local authorities, including health authorities, to avoid expulsion, and may also encounter added economic and linguistic difficulties. In French Guiana [8], foreigners and patients without residence permits also seemed more likely to be LFU. Indeed, socio-economic difficulties...
Therefore, they would also seem more likely to move elsewhere in
search of better living conditions or to go back to their country of origin.

In addition, immigrants are geographically mobile by definition.

May have led patients to rank medical follow-up low in their priorities
because we did not match our LFU data with National
authorities. A study by Couppié and colleagues in French Guiana [10]
showed that, before the availability of HAART, 48% of foreign HIV
patients returned to their country of origin. Although some patients
may have consulted a practitioner who is not included in the FHDH,
the increased risk of permanent loss to follow-up in untreated patients
and patients in the CDC category B stage suggests that some patients
died without benefiting from specialised care. There are numerous
definitions of LFU from HIV literature and the choice of a LFU
definition can affect the quality of study conclusions [11]. However, one
of the difficulties of the definition used in this study is that we could not
know for sure if patients LFU were still alive. This is why we looked at a
milder version of loss to follow-up defined as patients coming back after
more than 1 year. These patients may also have greater geographical
and social instability (finding a stable job or a stable partner).

The fear of being identified as HIV positive could be greater for those who are
still looking for a stable partner. In our study, due to low number of
indicated patients, it was impossible to analyse certain socioeconomic
variables such as residence permits and education. Patients are often
LFU at the early stages of infection and come back into the medical
circuit at very advanced stages of immunodepression, after a long period
of traditional "treatments." In a previous study [8], CD4 counts of more
than 500 per mm³ were associated with the temporary disappearance
of patients. This suggests that these patients may not feel any tangible
symptoms of HIV infection and thus do not perceive the benefits of
strict follow-up.

The above mentioned factors have also been shown to predict
appointment attendance in the United States [12]. The facts that treated
patients are less likely to be LFU and that patients in general have been
less likely to disappear since the availability of HAART suggest that
when patients understand the treatment benefits, they are more likely
to hope of improving their health. Physicians
should underline the importance of follow-up, especially if patients
do not receive treatment. Too often patients interrupt their follow up
yet are never contacted by the hospital, thus giving the impression that
the hospital does not notice. The most straightforward and perhaps
operationally feasible solution is to call every patient that does not show
at the consultation in order to give another appointment, thus keeping
and showing concern. Although the incidence of follow up
interruption has declined in recent periods, it was always highest in the
first months following care initiation. Therefore, new patients should
be of particular concern, and promptly recontacted when missing
appointments.

There are several limitations to the present analyses. Firstly,
the results found for a particular French clinical cohort cannot be
extrapolated to other locations, because risk factors for LFU may be
determined by the nature of the population, the place of residence, and/
or the methods of tracking and of keeping patients in care. Nevertheless,
several sociodemographic and clinical variables found here to be
associated with LFU seem to be common to many other studies.
Secondly, although chart information was updated some patients might
have been followed in another HIV centre in a different geographical
area. We may therefore have overestimated the incidence rate of LFU.
In addition, because we did not match our LFU data with National
Death Index registries, we may have considered deceased patients as
LFU. Thirdly, although the data for most of the sociodemographic and
clinical variables were prospectively collected, the study was designed
after data collection had ended.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Incidence rate (100 person-years)</th>
<th>Hazard ratio* (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>14</td>
<td>1.62(1.25-2.10)</td>
<td>0.000</td>
</tr>
<tr>
<td>30-40</td>
<td>8.6</td>
<td>1.40(1.10-1.72)</td>
<td>0.000</td>
</tr>
<tr>
<td>&gt;40</td>
<td>4.7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>1.05(0.89-1.30)</td>
<td>0.60</td>
</tr>
<tr>
<td>HIV diagnosis period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005-2008</td>
<td>2.5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1997-2004</td>
<td>7</td>
<td>1.15(0.92-1.42)</td>
<td>0.20</td>
</tr>
<tr>
<td>1988-1996</td>
<td>14</td>
<td>1.64(1.31-2.10)</td>
<td>0.000</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial CD4 &lt; 200/mm³</td>
<td>2.8</td>
<td>0.80(0.60-1.10)</td>
<td>0.082</td>
</tr>
<tr>
<td>Initial CD4 &lt; 200-499/mm³</td>
<td>7</td>
<td>1.10(0.92-1.13)</td>
<td>0.30</td>
</tr>
<tr>
<td>Initial CD4 &gt; 500/mm³</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>CDC categories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>6</td>
<td>0.78(0.63-0.79)</td>
<td>0.025</td>
</tr>
<tr>
<td>C</td>
<td>2.7</td>
<td>0.72(0.57-0.91)</td>
<td>0.006</td>
</tr>
<tr>
<td>Known drug use/addiction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>7.5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>10</td>
<td>1.80(1.20-2.80)</td>
<td>0.01</td>
</tr>
<tr>
<td>ARV therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAART+</td>
<td>3.9</td>
<td>0.24(0.19-0.30)</td>
<td>0.000</td>
</tr>
<tr>
<td>HAART-</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*Obtained using a Cox proportional hazard model including all the above mentioned
covariates.
CI: confidence interval; py: person-years

Table 2: Risk factors for temporary follow-up interruption of HIV-infected patients in Guadeloupe.

Figure 1: Kaplan-Meier estimates representing the survival function with follow up interruption as failure event, over time*1988-2008 hospital cohort in Guadeloupe (n=2732)*.
Conclusion

We attempted to quantify and identify predictors of follow up interruption of HIV patients in Guadeloupe. This information may help clinicians improve HIV-patient retention and thereby reduce morbidity and mortality, and promote risk reduction.

Acknowledgements

The authors would like to thank the members of the Guadeloupean HIV Cohort Study for data collection.

References

1. Infection à VIH et sida (2013) Base de données VIH.