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Incidence, Predictors and Reasons of Attrition of Patients on Antiretroviral Therapy for HIV in Eight Large-Cohort Sites in Conakry

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Abstract: *Introduction*: The purpose of this study was to estimate the incidence of attrition (death and lost to follow-up) among patients living with HIV on ART and to identify key predictors of this attrition. It also described the reasons why some patients are lost to follow-up. *Methods*: This was a historical cohort study of patients living with HIV put on ART between January 1, 2015 and December 31, 2020 in 8 large cohort sites in Conakry. An additional cross-sectional survey in the form of an investigation was conducted to describe the final status of patients reported lost to follow-up by the sites, as well as to describe the reasons for their loss to follow-up. Kaplan Meier techniques were used to estimate cumulative incidence, and the multivariate Cox proportional model was used to identify predictors of attrition. *Results*: The cumulative incidence of attrition was 19.50 over a median follow-up time of 2.5 years, for an overall attrition rate of 7.79 years per 100 person-years. Factors significantly associated with attrition were: Age 15 - 24 years [aHR = 2.212; 95% CI (1.321 - 3.704)], age >35 years [aHR = 1.723; 95% CI (1.041 - 2.852)], viral load >100,000 copies/ml [aHR = 2.056; 95% CI (1.668 - 2.534)], patients not on the 3-month or 6-month appointment system [aHR = 3.031; 95% CI (2.603 - 3.531)]. *Conclusion*: This study showed that the incidence of attrition increases with increasing follow-up time. Investigation of lost to follow-up reduced the estimated number of patients considered lost to follow-up and increased the number of deaths that were previously underreported. A prospective mixed study including many more variables would allow a better understanding of the attrition phenomenon among people living with HIV on ART in Guinea.

Keywords: Attrition, Reasons, Predictors, Antiretroviral Treatment, HIV/AIDS, Conakry

1. Introduction

The rapid expansion of antiretroviral therapy (ART) use has transformed the response to acquired immunodeficiency syndrome (AIDS) and has also had a significant impact on the health of people living with the human immunodeficiency virus (PLWH) [1]. Antiretroviral therapy has shown promising results in reducing HIV transmission, HIV/AIDS-

related morbidity and mortality [1]. Globally, more than 37.9 million people were living with HIV/AIDS in 2020. Two-thirds of these were in sub-Saharan Africa, and 24.5 million people on ART, 62% of whom were adults [2] Lifetime antiretroviral therapy is essential to optimize health outcomes for people living with HIV [3]. Retention in care is an essential element in achieving the second and third targets of the UNAIDS goals, namely that 90% of HIV-positive people are on antiretroviral treatment and 90% have a suppressed viral load [3]. In 2012, follow-up attrition was declared one of the major challenges of the next decade facing HIV care and treatment programs in resource-limited settings [3]. Wasting increases the risk of drug resistance and treatment failure in cases where death is not the cause of wasting [4]. Previous studies have shown that patients with treatment interruptions are more likely to develop treatment failure, viral rebound and clinically significant drug resistance [5]. Patients lost to follow-up at different stages of the HIV care cascade can increase HIV transmission, mortality, and morbidity rates as well as hinder efforts to control the HIV epidemic [6]. Wastage in HIV care is particularly common in low-income countries, where health systems and patients face many barriers to care [6]. Studies in sub-Saharan Africa have shown that the cumulative incidence of attrition after 3 years of follow-up can reach 35% [7]. A study in Uganda of patients who started antiretroviral therapy with a CD4 cell count > 350 cells/ml found that at 2.5 years, 20% of patients were lost to follow-up [8]. According to a study conducted in one of the sub-Saharan African countries, Uganda, the proportion of those lost to follow-up was 24.6% [9]. In various retrospective follow-up studies in Ethiopia, the incidence of lost to follow-up ranged from 8.2 to 11.6 per 100 person-years [10]. In Guinea, a study conducted on the problem of people lost to follow-up during treatment in the sites revealed a rate of lost to follow-up estimated at 47.7% [11]. At the national program and clinic level, failure to account for the lost can distort retention estimates and divert resources when planning and budgeting for HIV care [4].

The factors associated with attrition remain complex [4]. Previous studies have shown that younger or older age, male gender, single, divorced or separated marital status, illiteracy, lack of income-generating activity, non-disclosure of HIV diagnosis, stigma, low body mass index (BMI), distance from health facilities, poor nutrition normal body mass index, pregnancy, high or low CD4 count, advanced HIV infection (stage IV) (WHO classification), TB co-infection, type of ART regimen at the start of treatment, detectable viral load, and adverse effects of ART drugs were factors associated with attrition of patients on ART [4, 6, 9]. In Guinea, there are few studies on attrition of patients living with HIV from antiretroviral treatment sites. The few studies available on the subject are old and do not clearly address aspects related to the incidence and factors associated with attrition from the HIV care program (lost to follow-up of and death). It should also be added that previous studies did not take into account the investigation of lost to follow-up cases, which would lead to an overestimation of lost to follow-up and an underestimation of deaths. On this point, Martin W. G. Brinkhof et al, in a meta-analysis of studies based on tracing lost to follow-up, estimated a higher cumulative mortality ranging from 12% to 87% among patients lost to follow-up [12]. It is therefore important that data characterizing patient retention be available, particularly in routine health care delivery settings. It should be noted that most of the data currently available are derived from the implementation of tests and treatments in research settings [8]. The limitations of previous studies cited above motivated this study.

2. Methods

2.1. Setting

The study was conducted in eight (8) high-volume care sites for people living with HIV in Conakry, Republic of Guinea. In the Guinean context, a site is considered high-volume when the number of people on ART it manages is 250 or more. In 2019, 29 sites out of a total of 142 met this definition and managed more than 90% of all patients on ART in the country [13]. The present study focused on 8 high volume sites in the city of Conakry. These sites are: Communal Medical Center of Matam, Communal Medical Center of Flamboyants, Communal Medical Center of Coleah, Communal Medical Center of Minière, Health Center of Wanindara, Health Center of Tombolia, Health Center of Gbessia Port 1 and Health Center of Dabompa which are sites technically supported by the international NGO Doctors Without Borders of Belgium [14]. The choice of these eight sites is justified by the fact that they have electronic databases that allow for longitudinal analysis over a long period of patient follow-up. This is not easy in the other sites that do not have such a database, because in the latter, the individual medical records of the patients that are to serve as the main tool for data collection are generally not available in sufficient quantity and the few records that are available are generally not up to date.

As part of the follow-up to the World Health Organization (WHO) recommendations on antiretroviral treatment, in 2017 the country instituted the "Test - Treat" policy, i.e., initiate ART in all people who test positive for HIV [15]. For a better health coverage of people living with HIV, Guinea has made free since September 2007 (by joint decree of the Ministries of Health, Social Action and Economy and Finance) ART, anti-opportunistic infections, HIV screening, lymphocyte typing and viral load. This free HIV care is supported by the State and its technical and financial partners, including: The Global Fund, the NGO Doctors Without Borders of Belgium, the Community of Sant'Egidio, UNICEF, UNAIDS, the NGO Solthis, the World Health Organization, etc. The antiretroviral treatment administered to people living with HIV/AIDS in Guinea is a triple therapy generally combining two nucleotide reverse transcriptase inhibitors (NRTI) with a non-nucleotide reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI) or an integrase inhibitor (IG). According to the national HIV management protocol in

Guinea, all patients who test HIV positive should be put on ART regardless of their immune status (CD4 count and viral load level). Fixed combination therapies are favored in order to promote adherence and reduce the cost of care for the country. However, there are some patients who are on the second and third line of antiretroviral treatment.

2.2. Study Design and Data Sources

We conducted a historical cohort study in eight (8) high-volume HIV care sites in the city of Conakry. Data for estimating the incidence of attrition and identifying its predictors were extracted from the "TIER.NET" databases managed by ONG Doctors Without Borders of Belgium and exported to an Excel file.

An additional investigation in the form of a cross-sectional survey was conducted among patients considered lost to follow-up at these sites in order to determine their final follow-up status and to describe the reasons for this loss. To conduct this investigation, a data collection form was designed on the Kobocollect application. The lost-to-follow-up patients to be investigated were identified from a filter in the Excel file from the "follow-up outcome" column. Contacts for calls were obtained from the general registration records for ART treatment of HIV-positive patients. The modalities of this final status of the lost to follow-up were: deceased, self-transfer to another site, treatment dropouts or refusals, and actual lost to follow-up. Patients lost to follow-up who could not be reached and patients lost to follow-up who did not agree to provide information on their ART status were considered to be effectively lost to follow-up. This survey helped to address the problems of overestimation of lost to follow-up and underestimation of deaths among patients on ART.

2.3. Study Population and Sample Size

A retrospective chart review of patients followed in the 8 high-volume sites of Conakry from January 1, 2015 to December 31, 2020 was conducted for the analysis of clinical, para-clinical, and sociodemographic data of all included patients. All patients who tested positive for HIV after the two screening tests (Determine and Bioline) and were put on antiretroviral treatment in the 08 sites were considered as the study population. All adolescent patients aged 9 to 14 years and all adult patients aged 15 years and older at the time of initiation of antiretroviral therapy in the 8 high-volume sites of Conakry, with a documented date of initiation of triple antiretroviral therapy and a duration of at least 6 months on ART at the time of the end of the follow-up of the patients included in the study, were included in this study. The cut-off date is June 30, 2021. Excluded from this study were:

1) patients listed as having initiated ART during the study period and whose ART initiation date is unknown;
2) patients whose age of ART initiation is unknown;
3) patients who left the cohort and whose last appointment and/or event dates (lost to follow-up and death) are not known.

Exhaustive sampling was used to select all patients meeting the selection criteria from the primary tools and databases. Physicians responsible for the care of patients living with HIV were involved in identifying these patients.

2.4. Data Sources and Collection

For the realization of this study, data were collected from primary tools for managing clinical, para-clinical and socio-demographic data of patients (patient records, general registries, patient follow-up registries, pharmacy registries, and laboratory registries) and data compilation databases: Simplified Reproductive Model (SRM), Tracker, national viral load database and longitudinal patient follow-up databases. A data collection form will be designed on the Kobocollect application for the collection of data related to the follow-up survey of lost to follow-up patients.

2.5. Description of Variables

2.5.1. Dependent Variable

The dependent variable was attrition. Attrition was defined as the proportion of patients living with HIV who discontinued or stopped ART because they were considered lost to follow-up or deceased at the end of the study or at the time of data extraction. The deceased patient had the event of interest on the date of death; if this was not available, the date of last visit to the site was used. A lost to follow-up patient was any patient who had not attended the treatment site at least 3 months (90 days) after the date of their last clinical visit appointment and for whom no health status information was known before the date of data extraction. This definition was chosen to align with national guidelines for monitoring patients on antiretroviral therapy in Guinea. The lost to follow-up patient had the event on the date of the last clinic visit. A patient was considered censored if he or she had a formally recorded transfer to another site prior to data collection or was still being followed at the site at the end of the study period or at the time of data extraction.

2.5.2. Independent Variables or Predictors

Potential predictors or factors associated with attrition of patients on antiretroviral therapy were considered as independent variables in this study. The predictor variables analyzed consisted of:

1) Sociodemographic characteristics (patient gender, age, study sites, level of study site in the health care supply organization);
2) clinical characteristics (clinical stage of HIV infection according to the WHO classification);
3) para-clinical or biological characteristics (CD4 count, viral load);
4) therapeutic characteristics (antiretroviral treatment regimen, line of treatment, 3-month or 6-month appointment strategy).

2.5.3. Variables Related to Reasons of Attrition

These variables were collected by a complementary cross-sectional survey of patients reported lost to follow-up by the

sites concerned. The data collected concerned: the possibility of contacting the lost patient, the availability of the lost patient for questioning, the final status of the lost patient after the investigation (deceased, self-transferred, refusal of treatment, definitively lost) and the reasons for discontinuing treatment.

2.6. Data Analysis

The data entered in Kobocollect will be exported in an Excel file. They will then be imported into the IBM SPSS Statistics 25 software for analysis.

2.6.1. Descriptive Analysis

A descriptive analysis was performed on the entire study population as a first step. The results of the quantitative variables were described using the mean ± standard deviation. Quantitative variables whose distribution does not follow a normal distribution were described by the median and its interquartile range. Proportions with their 95% confidence intervals were estimated to describe qualitative or categorical variables. We used Kaplan Meir techniques to estimate the cumulative incidence of attrition or dropout (attrition and death) among patients on antiretroviral therapy at different follow-up periods.

2.6.2. Univariate Analysis

We plotted Kaplan Meier curves in the univariate analysis to assess attrition or dropout as a function of potential risk factors and the Mantel Heanszel log-rank test was used to compare risk curves. We used Cox univariate proportional regression to identify factors associated with attrition. The crude relative risk or hazard ratio (HR) and its 95% confidence interval were used as a measure of association. The patient inclusion period was 6 years, from January 1, 2015, to December 31, 2020. The date chosen for data extraction/collection was June 30, 2021; this represents the end date of the study. We calculated the duration of follow-up for each patient; this allowed us to estimate the median duration of follow-up for all patients. The difference between the event date and the inclusion date was the follow-up time for patients lost to follow-up, death, or transfer. The difference between the study end date and the initiation date was considered the follow-up time for patients who were still on antiretroviral therapy at the sites at the time of extraction or data collection.

2.6.3. Multivariate Analysis

Analysis of factors associated with dropout or attrition was performed using a multivariate Cox proportional hazards model. Analysis was performed not only for attrition but also for each of its components: lost to follow-up and death. This multivariate analysis was used to estimate the adjusted relative risk aHR (hazard ratio) and its 95% confidence interval for each factor retained. The proportional hazards assumption was evaluated using Kaplan-Meier plots against Cox predictions and the results of these analyses suggested that the proportional hazards assumption is valid. To identify independent associated factors of attrition, first variables were selected into the multivariable model based using a stepwise forward strategy (p value < 0.1). Moreover, sex and level of care were included based on their clinical and biological relevance in HIV-patient's retention in ART program. Second, stepwise backward elimination was used until all remaining variables were significantly associated with attrition (p value < 0.05). We also estimated the correlation between year of ART initiation and attrition.

3. Results

3.1. Description of the Sample

3.1.1. Patient Flow Chart

Between January 1, 2015 and December 31, 2020, 16439 patients diagnosed as HIV positive were put on ART at the 8 high-volume HIV care sites in Conakry. Of these patients, 10,473 met the inclusion criteria for this study. Of this study population, 2,371 (22.64%) patients were lost to follow-up, 1,448 (13.83%) patients were transferred to other sites for further management, 437 (4.17%) patients had died before data extraction, and 6,217 (59.36%) patients were actively on ART at the time of data extraction (figure 1).

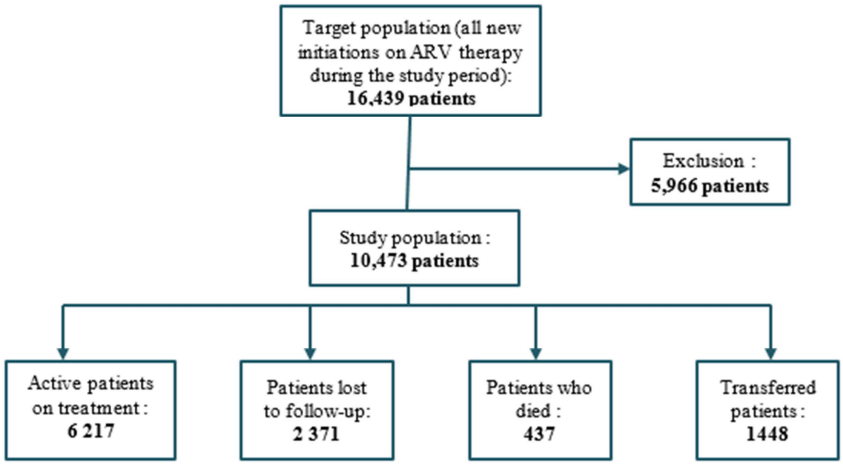

Figure 1. *Profiles of HIV/AIDS patients in the 8 sites of the large cohort in Conakry (January 1, 2015 to December 31, 2020).*

3.1.2. Basic Sociodemographic, Clinical and Biological Characteristics of the Study Population

Table 1. *Sociodemographic, clinical and para-clinical characteristics of the 10,473 HIV patients who initiated antiretroviral treatment between January 1, [2015] and December 31, 2020 in 8 high-volume sites in Conakry.*

Characteristics	Number	Percentage (%)
Site		
MCC of Coleah	696	6.65
MCC of Flamboyants	1281	12.23
MCC of Matam	2206	21.06
MCC of Minière	1254	11.97
HC of Dabompa	540	5.16
HC of Gbessia Port 1	1595	15.23
HC of Wanindara	1648	15.74
HC of Tombolia	1253	11.96
Site level		
Health center	5036	48.09
Hospitals	5437	51.91
Patient gender		
Man	2989	28.54
Women	7484	71.46
Median age (IQR)	34 years old (27 - 42)	
Age range		
< 14 years old	172	1.64
15 - 24 years old	1727	16.49
25 - 34 years old	3828	36.55
≥ 35 years old	4746	45.32
WHO stage of HIV infection		
Stage I	2705	25.83
Stage II	1214	11.59
Stage III	5867	56.02
Stage IV	679	6.48
Missing	8	
Median of CD4 count (IQR)	274 (135 - 444)	
Range of CD4 (cells/µl)		
<100	1493	14.26
100 - 200	1481	14.14
200 - 350	1898	18.12
> 350	2836	27.08
Missing	2765	
Mean ± SD of viral load	56381±408857	
Range of viral load (copy/ml)		
> 100,000	371	3.54
10,000 - 100,000	268	2.56
1,000 - 10,000	241	2.30
< 1000	5950	56.81
Missing	3643	
Basic ART regimen		
TDF + 3TC + EFV	9696	92.58
AZT + 3TC + NVP	223	2.13
Other regimens	554	5.29
On appointment at 3 months or 6 months		
Yes	7441	71.05
No	3032	28.95

ABC+3TC+ATV, ABC+3TC+DTG, ABC+3TC+EFV, ABC+3TC+LPV/r, AZT+3TC+ATV, AZT+3TC+DTG, AZT+3TC+EFV, AZT+3TC+LPV/r. Median follow-up time was 30.00 months (23.20 - 56.11), or 2.5 years

Data analysis was performed on a total of 10,473 patients enrolled in the 8 study sites. The Medical Communal Center (MCC) of Matam, with a legal status of Hospital, had the largest number of patients 2206 (21.06%). More than half of the patients, 5437 (51.91%), were followed up in hospitals, compared to 5036 (48.09%) in health centers. The female gender was the most represented with 7484 patients (71.46%). The median age of the patients was 34 years with an interquartile range (27 - 42). The most represented age group was ≥ 35 years with a headcount of 4746 (45.32). The majority of patients 9696 (92.58) were on the country's preferred regimen TDF+3TC+EFV. Stage 3 HIV infection was more represented with a headcount of 5867 or (56.02%). The median CD4 count was 274 cells per cubic millimeter with an interquartile range of (135 - 444). The highest CD4 count was >350 with a count of 2836 (27.08%). Among the patients on ART for at least 6 months, with a recorded viral load, 5950 (56.81%) patients had achieved virological suppression (VL<1000copies/ml). Of all the patients followed, 7441 (71.05%) patients were on the 1st line of ART.

3.2. Results of Patient Follow-Up

At the time of data extraction in the different databases, it was found that 2,371 patients out of 10,473 were considered lost to follow-up, i.e. 22.64%. An investigation, i.e. an "active search" for these lost patients was carried out by the psychosocial counsellors with the help of students in the final year of their medical studies (figure 2). At the end of this investigation, 1170 (49%) patients had dropped out of treatment, 432 (18%) of the patients had died, 462 (20%) had returned to treatment, 341 (13%) of the patients were silent transferees. Silent transferees are patients who were taking treatment at another site without the knowledge of the starting site.

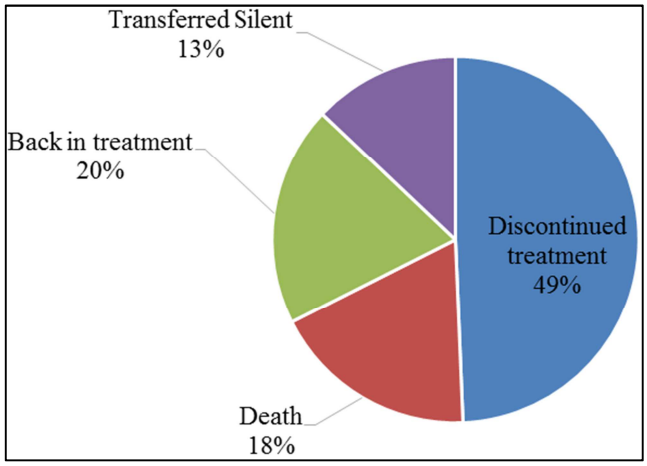

Figure 2. *Status of 10,473 patients followed in the 8 large cohort sites of Conakry from January 1, 2015 to December 31, 2020.*

Table 2. *Comparison of the follow-up of patients lost to follow-up on ART before and after the investigation in the 8 sites with a large cohort in Conakry from January 1, [2015] to December 31, 2020.*

	Before investigation of cases of lost to follow-up			After investigation of cases of lost to follow-up		
	Number	**Percentage (%)**	**95% CI**	**Number**	**Percentage (%)**	**95% CI**
From patient follow-up						
Lost to follow-up	2371	22.64	(21.79 - 23.48)	1171	11.18	(10.50 - 11.80)
Deceased	437	4.17	(3.82 - 4.53)	869	8.30	(7.80 - 8.80)
Transferred for follow-up elsewhere	1448	13.83	(13.18 - 14.49)	1754	16.75	(16.00 - 17.50)
Follow-up in site	6217	59.36	(58.37 - 60.35)	6679	63.77	(62.80 - 64.80)
Attrition						
Yes	2808	26.81	(26.00 - 27.64)	2040	19.50	(18.7 - 20.2)
No	7665	73.19	(72.22 - 74.07)	8433	80.50	(79.7 - 81.3)

Before the investigation, 2371 (22.64%) patients were considered as lost to follow-up, against 1171 (11.18%) patients identified as lost to follow-up after the investigation. Also, 437 (4.17%) patients were considered deceased versus 869 (8.30%) patients who died after the investigation. Patients transferred for management in another site were 1448 (13.83%) before the investigation, against 1754 (16.75%) of patients after investigation. 6217 (59.36%) patients were active before the investigation, against 6679 (63.77%) actually followed up at the end of the investigation. Thus, the attrition rate decreased from 26.81% before the investigation to 19.50% after the investigation (Table 2).

3.3. Reason for Loss of Patient Follow-Up

The follow-up survey focused on a total of 2,371 lost to follow-up patients. Of these patients we were able to reach 1,587 by telephone. The most frequently mentioned reasons for dropping out of treatment were: lack of food support 238 (15%), the health care facility is far from my home 175 (11.3%), I felt sick 167 (10.5%), I feel better 155 (9.77%) and patient displacement either for travel or moving 153 (9.64%). The reasons less mentioned were related to: I was made to pay for the examinations 12 (0.76%), lack of encouragement of the patient by a third person 33 (2.08%), discrimination in the site 36 (2.27%), frequent shortages of inputs in the sites 65 (4.1%). It should also be noted that 67 (4.2%) patients lost to follow-up reported not knowing if the treatment was lifelong. Lack of health improvement with ART 122 (7.69%), side effects of ART 107 (6.74%) were also reasons mentioned by the patients lost to follow-up (figure 3).

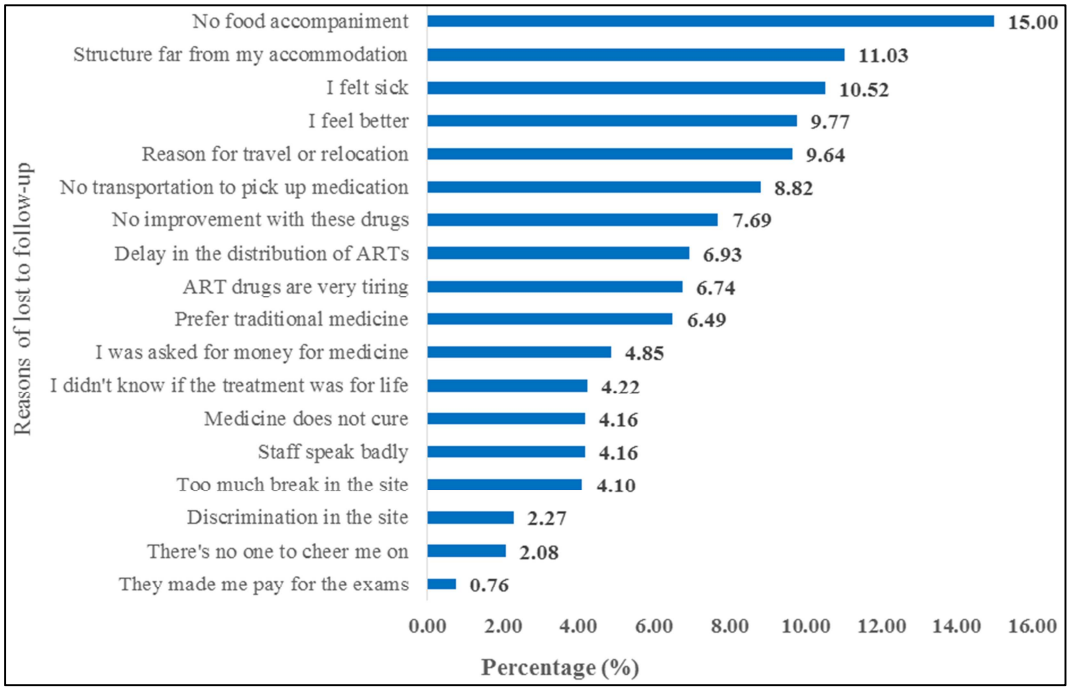

Figure 3. *Reason for loss to follow-up mentioned by the 1,587 patients contacted by telephone during the active search for patients lost to follow-up, in the 8 large cohort sites in Conakry from 1 January 2015 to 31 December 2020.*

3.4. Cumulative Incidence of Attrition at Different Patient Follow-Up Periods

The total follow-up time was 26,182.5 person years of observation. The median time of patient follow-up was 30 months (23.20 - 56.11) or 2.5 years. The overall attrition rate was 7.79 years per 100 person-years, with a mortality rate of 3.32 years per 100 person-years after investigation and a lost

to follow-up rate of 4.47 years per 100 person-years. In Table 3, we presented the cumulative incidence of attrition, lost to follow-up, and death at 6 months, 1 year, 2 years, 3 years, 4 years, 5 years, and 6 years.

Table 3. *Cumulative incidence and 95% interval of attrition (lost to follow-up or death) at 6 months, 1 year, 2 years, 3 years, 4 years, 5 years and 6 years of the 10,473 patients followed in 8 high volume sites in Conakry.*

Follow-up time	Cumulative incidence (95% CI)		
	Attrition	Lost to follow-up	Death
6 months	6.72 (6.47 - 6.97)	3.90 (3.70 - 4.09)	2.93 (2.76 - 3.10)
1 year	11.19 (10.86 - 11.51)	6.43 (6.17 - 6.68)	5.08 (4.85 - 5.32)
2 years	17.68 (17.26 - 18.09)	10.62 (10.28 - 10.97)	7.89 (7.59 - 8.19)
3 years	22.25 (21.77 - 22.73)	13.43 (13.02 - 13.83)	10.18 (9.82 - 10.54)
4 years	25.84 (25.29 - 26.38)	15.59 (15.12 - 16.05)	12.14 (11.71 - 12.56)
5 years	29.11 (28.47 - 29.75)	18.19 (17.62 - 18.77)	13.34 (12.85 - 13.83)
6 years	31.60 (30.76 - 32.45)	19.73 (18.99 - 20.46)	14.79 (14.08 - 15.50)

3.5. The Kaplan Meier Curve in Univariate Analysis and the Log Rank Test

In figure 4, it can be seen that the attrition incidence curve for males is higher than that for females. Also the attrition incidence curve for children under 15 years (0 - 14 years) is higher than that of adults. It is also noted that the attrition incidence curve for patients who started ART at stage IV of HIV infection is higher than for other patients. The same is true for patients who started ART with low Cd4 levels compared with others (figure 4). Indeed, the incidence of attrition in men was higher than in women (21.1% versus 18.8%; with log rank test p=0.00016). According to age, the incidence of attrition was more accentuated in patients with an age between 0 - 14 years i.e. 25.4% versus 18.4% in patients with an age between 15 - 25 years, 18.3% in patients with an age ≥ 35 years. Patients with CD4 count < 100 cells/µl were more prone to attrition 24.8% vs 21% for patients with CD4 count 100 - 200 cells/µl, 18.7% for patients with CD4 count 200 - 350 cells/µl and 17.7% for patients with CD4 count > 350 cells/ µl. The incidence of attrition was also higher in patients with stage III and IV HIV infection with 20.8% and 24.2% respectively compared to 16.2% and 17.7% for stage I and II of the WHO classification of HIV infection. Patients on an AZT+3TC+NVP-based regimen were more exposed to attrition (29.1%) compared to patients on TDF+3TC+EFV regimen (19.5%).

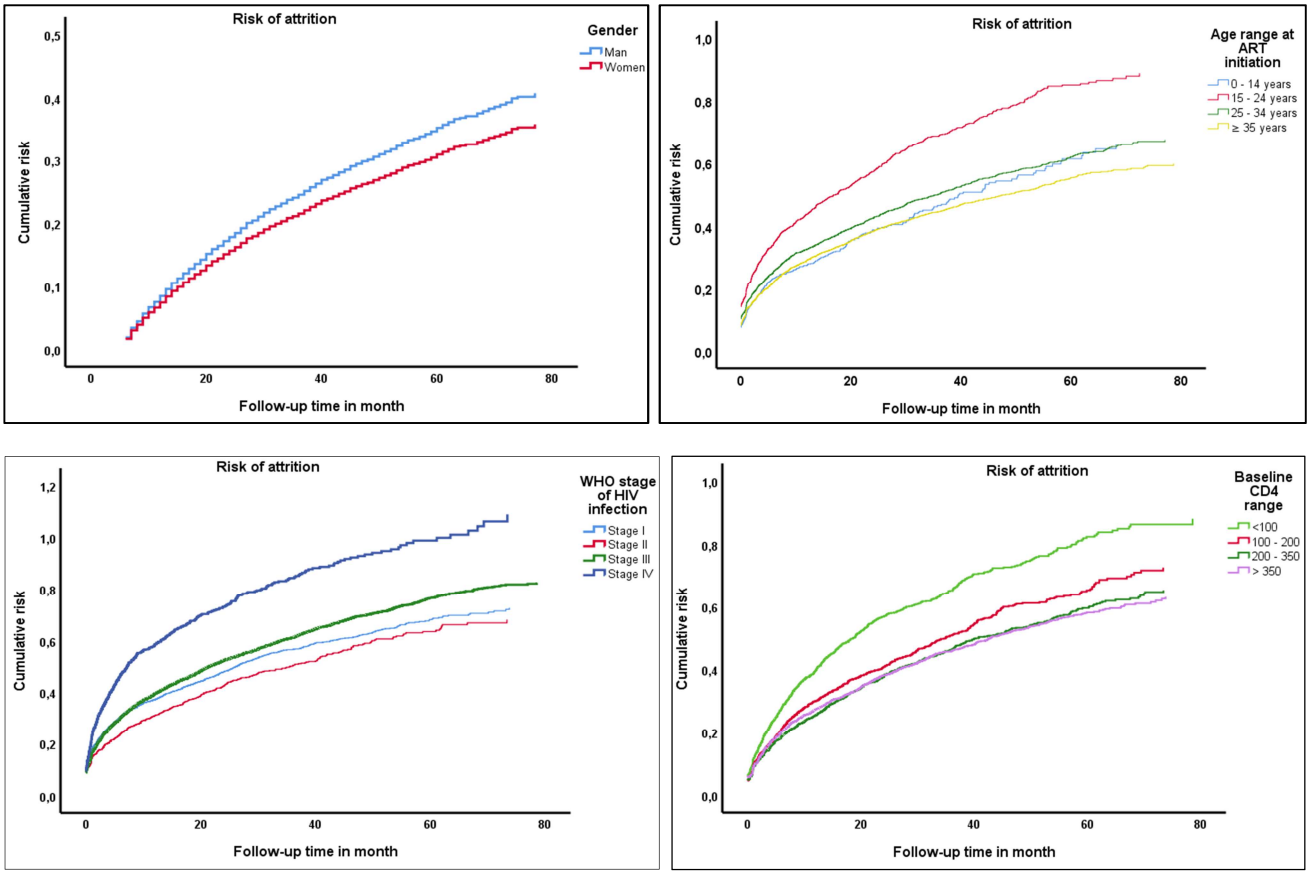

Figure 4. *Cumulative incidence of attrition by selected characteristics of patients followed in the 8 large cohort sites in Conakry from January 1, 2015 to December 31, 2020.*

3.6. Multivariate Cox Analysis

In the multivariate Cox analysis, factors significantly associated with attrition were: Age 15 - 24 years [aHR = 2.212; 95% CI (1.321 - 3.704)], age >35 years [aHR = 1.723; 95% CI (1.041 - 2.852)], viral load >100,000 copies/ml [aHR = 2.056; 95% CI (1.668 - 2.534)], patients not on the 3-month or 6-month appointment system [aHR = 3.031; 95% CI (2.603 - 3.531)]. Factors associated with lost to follow-up were: 15 - 24 years of age [aHR = 3.023; 95% CI (1.321 - 6.917)], 25 - 34 years of age [aHR = 2.272; 95% CI (1.003 - 5.145)], patients with age > 35 years [aHR = 2.404; 95% CI (1.065 - 5.429)], viral load > 100,000 copies/ml [aHR = 1.497; 95% CI (1.106 - 2.026)], patients not on the 3-month or 6-month appointment system [aHR = 2.599; 95% CI (2.132 - 3.169)].

Factors significantly associated with death were: viral load >100,000 copies/ml [aHR= 2.810; 95% CI (2.075 - 3.804)], viral load 10,000 - 100,000 [aHR=1.681; 95% CI (1.142 - 2.476)], patients not on the 3-month or 6-month appointment system [aHR= 3.814; 95% CI (2.994 - 4.860)] (Table 4).

Table 4. *Multivariate analysis of factors associated with attrition, loss of follow-up, and death of patients followed in the 8 high-volume sites of Conakry from January 1, 2015 to December 31, 2020 of the Cox regression.*

Characteristics	Attrition		Lost to follow-up		Death	
	aHR (95% CI)	p-value	aHR (95% CI)	p-value	aHR (95% CI)	p-value
Sites						
MCC of Coleah	0.569 (0.403 - 0.805)	0.001	0.560 (0.356 - 0.879)	0.012	0.594 (0.347 - 1.017)	0.057
MCC of Flamboyants	0.869 (0.672 - 1.124)	0.286	0.998 (0.723 - 1.376)	0.989	0.681 (0.442 - 1.049)	0.082
MCC of Matam	0.783 (0.605 - 1.013)	0.063	0.805 (0.576 - 1.125)	0.204	0.742 (0.496 - 1.113)	0.149
MCC of Minière	1.254 (0.993 - 1.585)	0.058	1.321 (0.978 - 1.782)	0.069	1.204 (0.828 - 1.752	0.331
HC of Dabompa	1 (*reference*)		1 (*reference*)		1 (*reference*)	
HC of Gbessia Port 1	0.748 (0.485 - 1.156)	0.191	0.792 (0.459 - 1.366)	0.401	0.699 (0.341 - 1.436)	0.33
HC of Wanindara	0.684 (0.527 - 0.887)	0.004	0.561 (0.393 - 0.802)	0.002	0.849 (0.574 - 1.253)	0.409
HC of Tombolia	0.932 (0.735 - 1.183)	0.563	1.086 (0.805 - 1.466)	0.589	0.736 (0.497 - 1.091)	0.127
Range of Age						
< 15 years	1 (*reference*)		1 (*reference*)		1 (*reference*)	
15 - 24 years old	2.212 (1.321 - 3.704)	0.003	3.023 (1.321 - 6.917)	0.009	1.833 (0.941 - 3.572)	0.075
25 - 34 years old	1.580 (0.951 - 2.623)	0.077	2.272 (1.003 - 5.145)	0.049	1.206 (0.626 - 2.323)	0.575
≥ 35 years old	1.723 (1.041 - 2.852)	0.034	2.404 (1.065 - 5.429)	0.035	1.347 (0.705 - 2.575)	0.367
Range of viral load						
> 100,000	2.056 (1.668 - 2.534)	< 0.001	1.497 (1.106 - 2.026)	0.009	2.810 (2.075 - 3.804)	< 0.001
10,000 - 100,000	1.290 (0.983 - 1.694)	0.067	1.018 (0.691 - 1.501)	0.927	1.681 (1.142 - 2.476)	0.008
1,000 - 10,000	1.264 (0.951 - 1.681)	0.107	1.163 (0.798 - 1.695)	0.433	1.427 (0.921 - 2.211)	0.112
< 1000	1 (*reference*)		1 (*reference*)		1 (*reference*)	
On appointment at 6 months or at 3 months						
Yes	1 (*reference*)		1 (*reference*)		1 (*reference*)	
No	3.031 (2.603 - 3.531)	< 0.001	2.599 (2.132 - 3.169)	< 0.001	3.814 (2.994 - 4.860)	< 0.001

4. Discussion

The purpose of this study was to estimate the incidence of attrition among patients on ART by taking into account missed deaths among patients reported lost to follow-up by the sites.

Thus, the overall incidence of attrition was 7.79 years per 100 person-years, with a mortality rate of 3.32 years per 100 person-years after investigation and a lost to follow-up rate of 4.47 years per 100 person-years. This attrition result corroborates with that found in studies in northeastern Ethiopia and Uganda, which reported attrition rates of 8.36 years per 100 person-years and 7.5 years per 100 person-years respectively [2, 8].

This result of our study could be explained by the set of strategies newly implemented by the NGO Doctors Without Borders in collaboration with the National Program for the Fight against HIV/AIDS and Hepatitis, in particular the recruitment and training of psychosocial agents who carry out therapeutic education in these sites, the reminder of patients who are late for an appointment, the search for patients who have been lost to follow-up, but also home visits. All these strategies contribute to patient retention in treatment.

The results of the investigation showed a decrease in the proportion of patients lost to follow-up from 2,371 (22.64%) to 1,171 (11.18%), an increase in the proportion of deaths from 437 (4.17) to 869 (8.30). This could be explained by the behavior of some patients who leave their usual care site for another site without informing their usual site. We defined this event as a silent transfer. It should also be remembered that some patients who are lost to follow-up may have died without the usual care site being informed, and the usual care site continues to consider them as lost to follow-up, yet they are not. Rather, they are deceased. Hence the need for routine investigation of lost to follow-up cases to update statistics on lost to follow-up and deaths.

The incidence of attrition was higher in men than in women. These findings are consistent with those of a study

conducted in Ethiopia at Karamara General Hospital in the city of Jigjiga [1]. This could be explained by the fact that the men often move to the mining areas in search of work, thus abandoning the treatment. This patient does not inform the care structure to allow their transfer to the sites in the area of relocation. Also, HIV testing is late among men who most often consult at an advanced stage of the disease, which also leads to cases of attrition (lost to follow-up or community death).

The incidence of attrition was also high in patients with stage III and IV HIV infection compared to patients diagnosed with stage I and II HIV infection. This finding is similar to a study conducted in Uganda, North East and North West Ethiopia which also reported that patients with stage III and IV HIV infection were more susceptible to attrition [2, 8, 10]. This could be explained on the one hand by the fact that at these stages opportunistic diseases occur. This leads patients to resort to traditional medicine for treatment and thus abandon ART. On the other hand, the lack of adequate management of the disease in these centers leads to community deaths of patients. In our study, patients in stage IV of HIV infection were less prone to attrition as a result of patients' detour to traditional medicine and their return to NGO Doctors Without Borders Belgium facilities, which offer free care to patients in the late stages of the disease.

The incidence of attrition was also very high among patients on an AZT+3TC+NVP-based regimen compared to the TDF+3TC+EFV-based regimen. This result is consistent with a study conducted in Ethiopia at the University of Gondar [9]. This could be explained by the dosage of the drug (twice a day), which means that with all the side effects, patients do not take the product correctly and this leads to loss of follow-up.

Following interviews with the patients lost to follow-up, we noticed that most of the patients lost to follow-up were not sufficiently informed about the importance of antiretroviral drugs. The main reason most mentioned was the lack of nutritional support (15%). It should be noted that at the beginning of HIV treatment by NGO Doctors Without Borders Belgium in Guinea, patients followed up in the sites supported by this NGO benefited from food support as a source of motivation to keep their appointments. The end of this project contributed to the loss of follow-up for many patients treated at these sites. The distance of the treatment facility from the patients' homes (11.03%) was also noted as a reason for abandoning treatment. This reason was related to the cost of transportation that the patient would have to pay to get to the facility. Transportation costs are a barrier to care, as they often compete with other costly demands such as food, housing or school fees, thus compromising access to care [16]. I felt sick (10.52%) was also a reason mentioned, as patients who had preferred traditional medicine to ART were increasingly sick, making it difficult to travel to the care sites as they had not disclosed their status to the family member. Patients who also felt better after taking ART and who discontinued treatment returned in a condition that required hospitalization.

In this study, age, viral load and differentiated management (3-month and 6-month appointment system) were associated with attrition and its components. Indeed, being young (15 - 24 years) increased the risk of attrition by 2.2-fold compared with the age group 25 - 34 and ≥ 35 years. This could be explained by the fact that young people are difficult to track because for the most part they do not believe in the existence of the disease; with an improvement in health they drop out of treatment. Young people are also afraid of the stigma and discrimination that can result from being HIV positive.

In our study, failure to suppress viral load (VL > 100,000 copies/ml) increased the risk of attrition by 2.05 times and the risk of death by 2.81 times. Viral load is inversely proportional to CD4 count and proportional to stage of infection. As the viral load increases, the CD4 count decreases and leads to the occurrence of opportunistic infections. The severe immune deficiency generated, associated with the appearance of opportunistic diseases, which are more frequent at these stages, leads to the patient's bed rest, traditional medicine and finally the death of the patient in the community.

The results of our study showed that the risk of attrition was 3.03 times higher in patients not enrolled in the 3-month and 6-month appointment system compared to those enrolled. This system, which is intended for normally adherent patients, reduces the frequency of patient visits to treatment sites, thereby reducing all the expense and stigma associated with taking ART.

This study has a number of limitations. Since some socio-demographic variables were not included in the database, such as marital status, occupation, and clinical variables such as opportunistic diseases, we were unable to include them in the analysis. This situation could be explained by the breakdown and poor management of patient records. In addition, this study did not include patients from the interior of the country. The economic, socio-demographic and geographic context of the interior, which is slightly different from that of Conakry, could influence the attrition of patients on antiretroviral treatment differently. However, the fact that it was conducted in Conakry, where more than 50% of the national cohort of people living with HIV in Guinea are cared for, provides a basis for a nationwide study on the investigation of attrition in Guinea. In addition, the fact that it involved more than 10,000 patients means that this study has good sampling power and is representative of the cohort of people on ART in Conakry, if not the entire country.

5. Conclusion

This study showed that the incidence of attrition increases with time of follow-up. The investigation of lost to follow-up cases reduced the estimated number of patients considered lost to follow-up. It also increased the number of deaths that were previously underreported. A prospective mixed-methods study with many more variables would provide a better understanding of attrition among people living with

HIV on ART in Guinea. In the meantime, we recommend that the national AIDS control program Strengthen nutritional support for HIV patients on ART, routinely conduct investigations of lost to follow-up cases, make data management tools available and implement a results-based motivation/financing mechanism for health care providers to improve the quality of care for people living with HIV (data quality management and tools, monitoring of treatment failures, improvement of patient retention in the ART treatment program, monitoring of early warning indicators in the context of HIV care, etc.).

List of Abbreviations

HIV, Human Immunodefiency; ART, Antiretroviral Treatment; CD4, Cluster of Differentiation; AIDS, Acquired Immunodeficiency Syndrome; PLHIV, People Living with HIV; NGOs, Non-Governmental Organization; WHO, World Health Organization; MCC, Medical Communal Center; HC, Health Center; IQR, Interquartile Range; SD, Standard Deviation; aHR, Adjusted Hazard Ratio.

Declarations

Ethical Approval and Consent to Participate

For data collection, authorization from the national HIV/AIDS and Hepatitis program was obtained through a letter of approval. This is simply a programmatic performance evaluation study of Guinea's national AIDS and hepatitis program. It was conducted by a candidate in the Master of Public Health program at the University of Aix Marseille, SESSTIM in France. The protocol for this study was validated by the supervisory team of this Master's program before data collection. Verbal consent was obtained from site managers prior to data collection. Informed consent was obtained from the lost patients prior to the interview. Arrangements were made to ensure the confidentiality of information about the identity of patients included in our study.

Availability of Data and Materials

The data used in the study are not publicly available. Anyone wishing to obtain these data for scientific purposes may request them from the authors of this work.

Competing Interests

The authors stated that there is no competing interest.

Consent for Publication

Not applicable.

Authors' Contributions

Niouma Nestor Leno, Study Design, data analysis and manuscript drafting; Jean Michel LAMAH, Study Design, data analysis and manuscript drafting, Foromo Guilavogui, Manuscript reviewing; Thierno Saidou DIALLO, Manuscript reviewing; Youssouf KOITA, Manuscript reviewing; Laye Kaba, Manuscript reviewing; Arnold AHIATSI, Manuscript reviewing; Nagnouman TOURE, Manuscript reviewing; Souleymane CHALOUB, Data collection and manuscript reviewing, Andre KAMANO, Data collection and manuscript reviewing; Mahamadou DRABO, Review of study design and validation of data analysis; Jean GAUDART, Review of study design and validation of data analysis.

Competing Interests

The authors stated that there is no competing interest.

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