

Original Research Article

Factors favoring non-compliance of treatment to People living with HIV/AIDS in General Reference Hospital of Gbadolite, Nord Ubangi, Democratic Republic of the Congo

Abstract

Background

ART is one of the important pillars of the fight against AIDS. It restores immunity and reduces the risk of death. Its success lies in its strict compliance while its non-compliance exposes to the risk of resistance and therapeutic failure. The objective of this study was to determine the factors associated with the non-compliance to ART of PLWHA monitored at the General Reference Hospital of Gbadolite.

Methodology

It was an analytical cross-sectional study conducted between December 2017 and January 2018. The compliance was measured from patient reports and by counting the number of tablets remaining from the current month of the survey. Any PLWHA who failed to take their medication at most 2 times during the month preceding the survey or whose number of remaining tablets was greater than the expected number based on the month's consumption was considered non-compliant. In total, 208 participants were selected based on the established selection criteria and several factors which led to the non-compliance of the treatment.

Chi-square and logistic regression were used to determine the associations between factors and the non-compliance. All tests were performed at the threshold of $\alpha=0.05$.

Results

In fact, 280 PLWHA had participated in the survey. The mean age was 38.7 ± 7.2 years while the prevalence was 51.1%. Following gender, female accounted as non-compliant (65.7 %) than male. The main reasons for the non-compliance to treatment were as follows: the order of frequency, medication breakdown, lack of food, forgetting, side effects, travel and fasting. Factors associated with the non-compliance were loneliness in marital status ($p=0.000$; OR=18.6, CI (8.926 - 38.574)), revival church religion ($p=0.002$; OR=9.2 ; CI (2.245 - 37.449)), low level of knowledge of ART principles ($p=0.005$; OR=1.4; CI (1.169 - 2.735)) and lack of knowledge of ART duration ($p=0.021$; OR=1.7 and CI (1.020 - 2.829)).

Conclusion

The objective of this study was to determine the factors associated with the non-compliance of ART. The factors found in this work were those that had been found at different levels of association by many authors in previous work, namely marital status, religion, low level of knowledge about ART and lack of knowledge of duration of ART.

Keywords: Non-compliance, ART, HIV, Gbadolite, DRC

Introduction

Discovered since the 1980s, the human immunodeficiency virus (HIV) is probably the most studied virus in history to date. HIV infection, a global scourge, remains a major public health problem to date [1].

Having a high prevalence worldwide, with over 35 million deaths, HIV infection remains incurable up to now. It has become the pandemic of the century with 36.7 million people living with HIV worldwide until December 2016. An estimated 4 932 people were infected daily with HIV, thus a total of 1.8 million new HIV cases globally at the end of 2016. Pending the same year, about 2 740 people died of AIDS-related infections every day, and this corresponds to a total of 1 million deaths in the world. Nevertheless, with the efforts of governments around the world, data on the HIV epidemic show that the number of new infections has fallen by 16% since 2010 and that AIDS-related deaths have fallen by 47.3% since 2005 [2].

Sub-Saharan Africa is the most affected by the epidemic with around 25.6 million PLWHA or 70% of cases worldwide [3]. African countries with limited resources fight efficiently against this outbreak of which the largest number of deaths from HIV-related infections is still increasing. However, according to the UNAIDS and WHO report on the fight against AIDS, significant progress has been made in Africa and is encouraging for the continent's governments. In 2014, there was a 41% drop in new infections compared to 2000 and a 34% drop in deaths due to HIV infection [4-5].

The Democratic Republic of the Congo (DRC) has a generalized type of outbreak with an overall prevalence of 1.2%. The distribution of infection is not uniform across the country, varies from one province to another; ranging from Maniema the most affected province with 4.0% to the former province of Bas-Congo (currently Kongo Central) with 0.2%. The seroprevalence of this infection is higher among women (1.6% among pregnant women) than men (0.6%) [6]. The number of people living with HIV is estimated at 381 187, including 42 145 children under 15 years old and 224 673 women. Estimates for 2016, showed that new infections are estimated at 38% among young women of childbearing age (15-24 years), 20% of AIDS-related deaths were among children under 15 years old with low access to early detection and paediatric ART (17%) while 157 072 PLWHA were under treatment (41.2%) [7-8].

The former province of Equateur, from which the new province of Nord-Ubangi emerged, had a prevalence of 0.6% according to the 2013-2014 EDS-II report. As seroprevalence for the new provinces has not yet been determined, the province of Nord-Ubangi still shares the same prevalence as the Greater Equateur with the same socio-economic and cultural contexts. This province has only 3 health zones with the AIDS control package out of a total of 11 health zones.

The General Referral Hospital of Gbadolite, in the health zone of Gbado-lite has integrated the medical care of PLWHA since 2004 and currently has more than 300 PLWHA enrolled in antiretroviral treatment [9]. Although there is no cure for HIV infection nowadays, antiretrovirals have been developed to slow the progression of the disease and allows to lengthen the lifespan of infected people. Before the discovery of antiretrovirals, the history of the HIV epidemic was characterized by alarming statistics, dominated by an increasing number of new infections and deaths. For example, in 1999, new infections worldwide were around 5.4 million of which 4 million in sub-Saharan Africa [11]. With the advent of effective therapy with combinations of the three antiretroviral molecules, the HIV epidemic has seen a turning point in its history in terms of positive developments in the fight against this pandemic. Since 1996, these new approaches have revolutionized the treatment of the disease, making viral load in the blood undetectable and thus preventing the evolution of AIDS [11]. In contrast, multidrug antiretroviral therapy enables PLWHAs to live productive and healthy lives. In order to halt the spread of the HIV epidemic and improve patients' comfort, several countries have developed control strategies, including the availability of effective antiretroviral drugs that significantly reduce HIV-related mortality [12-13].

By the end of 2015, just over 17 million of PLWHA were on ART worldwide. While in May 2016, the UN Secretary-General revealed in a report that the extraordinary progress made over the past 15 years could be lost and encouraged all partners to commit their energies to increase investments in order to end the AIDS epidemic as a threat to public health [14]. To make the riposte advanced, the World Health Organization (WHO) has developed the 2016-2021 Global Health Sector Strategy for HIV with a number

of targets to be achieved by 2021, of which reducing the number of HIV infections to less than 500,000; zero new infections in infants; reducing the number of deaths to less than 500,000 and the famous 90-90-90 (90% of people living with HIV tested; 90% under treatment; viral load suppression in 90% of people under treatment) [15]. The extension of ART to all PLWHA and the development of prevention options can help achieve these targets and prevent 21 million AIDS-related deaths and 28 million new infections by 2030. This motivated WHO to recommend that any suspected case to be placed under ART as soon as they tested positive. Several studies and research have shown that if an HIV-positive person complies with an ART regimen, the risk of transmission of the virus to a healthy sexual partner can be reduced by 96%. WHO recommendations to start ART for anyone with HIV will contribute to a significant reduction in HIV transmission [12, 17].

For this to happen, the success of treatment depends on the ability of PLWHA to take the drugs correctly while respecting the time required to take the medication and the duration of treatment, which must be for life. Poor compliance to treatment leads to the therapeutic failure and therefore to the development of viral drug resistance [18-19]. ART has changed the management of HIV infection, transforming the perception of the disease and this infection has become a chronic disease that can be lived with [20]. The notion of chronicity of HIV infection introduces the notion of compliance to the management of treatment; a problem that surrounds the management of chronic diseases [20]. WHO defines the compliance as "the extent to which a person's behaviors in taking a drug, diet and/or lifestyle change correspond to the recommendations of a health professional" [21]. It refers to the adequacy between the patient's behavior and the proposed treatment.

The non-compliance constitutes the total or partial absence of this matching between the patient's behavior and the proposed treatment. It is determined by several factors related either to the nature of the treatment or to the socio-economic and psychological factors of the patient, the patient-caregiver relationship and socio-cultural factors [22-23]. Non-compliance leads to the therapeutic failure in the context of antiretroviral treatment. It is cited by WHO as one of the determinants of treatment failure and HIV resistance to antiretroviral drugs [19]. In ART, compliance of at least 95% is essential for therapeutic success: lowering the viral load, which must become undetectable, restoring immunity and improving clinical health. Compliance below 95% leaves a window for virological escape leading to therapeutic failure [24-25].

The General Referral Hospital of Gbadolite, located in the health zone of Gbado-lite in Nord-Ubangi province, has integrated the medical care of PLWHA since 2004 and now has just over 272 patients enrolled in care. The 2016 annual report showed that 37 of them had failed treatment (14%), 35 were lost (13%) and nine deaths (4%). Although no compliance studies have yet been conducted in the area, non-compliance could be a factor in these results [9].

Since the integration of a medical care package for PLWHAs in this health zone, studies on patient compliance with ART have yet been carried out neither in Nord Ubangi province nor in the health zone of Gbado-lite. Motivated by the factors associated with PLWHA non-compliance with ART, we chose to conduct this study in order to improve the management of these patients. The knowledge of these factors would help in the amelioration of the management of PLWHA in the concerned health zone insofar as such it would allow to the caregiver to respect it while consulting.

The main purpose of this study was to evaluate the determinants of non-compliance of ART amongst PLWHA monitored at the General Reference Hospital of Gbado-lite.

2. Material and methods

2.1 Study area, Study design and statistical units

The study was carried out at the General Referral Hospital of Gbado-lite located in the urban-rural health zone of Gbado-lite in the province of Nord-Ubangi between September 1st and December 31st, 2017. The study was of the transversal type with an analytical focus.

They consisted of PLWHA on ART for at least 7 months and were followed at the General Reference Hospital of Gbado-lite.

2.2 Sample size

The sample size for this study was estimated using the formula

$$n \geq \frac{Z_{\alpha}^2 p(1-p)}{d^2}$$

For this work, the rate of the non-compliance with ART ranged between 27% and 58.5% with an average of 44%, this average was used as per the literature requirements of similar studies. The p is equal to 0.44 and 1-p equals 0.56.

Then, the formula is as follows:

$$n \geq \frac{(1,96)^2 \times 0,44 \times 0,56}{(0,05)^2} = 379$$

Z at the 5% threshold is equal to 1.96 and d = 0.05, the formula gives the size of 379.

As this health structure had only 280 PLWHA enrolled in the care service, all were included in the study.

2.3 Sampling technique

Because the number of PLWHA enrolled in the PEC service at the GRH of Gbadolite was lower than our calculated sample size, there was no question of using any sampling technique. All PLWHA were included in the study.

2.4 List and operational definitions of variables

2.4.1. List of variables

- Dependent variable: Non-compliance with antiretroviral treatment
- Independent variables:
 - Socio-demographic characteristics (age, sex, occupation, level of education, marital status, religion)
 - Place of residence
 - Socio-economic level
 - Stigmatization
 - Type of therapeutic combination
 - Antiretroviral drugs out of stock
 - Sharing information about HIV status with family members
 - Presence of opportunistic infections
 - Sensation of clinical healing
 - The use of traditional treatment
 - Psycho-social support
 - Quality of the patient-caregiver relationship
 - Adverse drug reactions
 - Alcohol, tobacco or other drug poisoning
 - Processing time

2.4.2. Operational definition of variables

Dependent variable : Non-compliance with ART. This is the failure to take medication for at least 2 days over a period of 30 days of treatment, or failure to respect treatment schedules. Skipping days without taking the treatment. It indicates the extent to which the patient is not following the treatment plan.

- **Variables on socio-demographic characteristics**

- Age: this is the age of the respondent at their last birthday. It was collected at the interval scale
- Sex: This is the respondent's gender. It was collected at nominal scale and coded as 1 = Male and 2 = Female
- Marital status: This is the respondent's civil status. It was collected at nominal scale and coded as: 1. Married 2. In a common-law relationship 3. Divorced 4. Widowed 5. Single. The variable was categorized after collection into 1. living in a couple and 2. Those living alone
- Religion: This is the church to which the respondent belongs. Is nominal and codified in 1: Catholic, 2. Protestant, 3. Kimbanguist, 4. Islamic, 5. Armée du salut, 6. Revival Church
- Occupation: The respondent's daily or income-generating activity; it was collected at nominal scale and codified into 1. state official, 2. trader, 3. student, 4. taximan (cyclist toleka), 5. housewife, 6. soldier, 7. farmer, 8. no occupation. After collection, it was categorized as 1. with occupation and 2. No occupation
- Educational level: The highest level of education attained by the respondent. It was collected at the nominal scale and codified into 1. no level, 2. primary, 3. secondary, 4. higher. After collection, it was categorized into 1. low-level education and 2. High level of education
- Socio-economic level: It is the respondent's standard of living in relation to what he earns from his occupation. It was collected at nominal scale and then rated and categorized into 1. low socio-economic level, 2. high socio-economic level.

- Variables related to ART

- The type of combination therapy: Drug combination used by the respondent. It was collected at nominal scale and codified into 1. D4T+3TC+NVP ; 2. AZT+3TC+NVP ; 3. TDF+3TC+EFV ; 4. D4T+3TC+EFV ; 5. AZT+3TC+LPV/r and 6. ABC+ddI+LPV/r
- Presence of Adverse Reactions: Existence in the respondent of abnormal clinical events secondary to taking medication. It was collected at nominal scale and coded into 1. Yes and 2. No.
- Processing time: This is the time elapsed between the start of ART and the day of the survey. It was collected at the interval scale. After collection, it was categorized as 1.

- Processing time: This is the time elapsed between the start of ART and the day of the survey. It was collected at the interval scale. After collection, it was categorized into 1. 5 years or less and 2. More than 5 years.

- Knowledge of the respondent: This is all the essential information known to the respondent on ART.

- Variables related to the socio-cultural environment

- Sharing HIV status with family members: Informing other family members of your HIV status. Collected at nominal scale and codified 1. yes and 2. No
- Psycho-social support: Existence of social structures to support PLWHA. Collected at nominal scale and codified in 1. Yes and 2. No
- Stigma: A socio-cultural habit of indexing PLWHA because of their HIV status.

- Variables related to the organization of the PEC structure

- Out of stock of drugs: Absence of AVRs of more than 3 days at the HGR. It was collected at nominal scale and codified into 1. Yes and 2. No
- Geographical inaccessibility: Distance of more than 10 km between the residence of PLWHA and the PEC structure. It was collected at nominal scale and codified into 1. Yes and 2. No

2.5. Data collection

Data were collected in households by interviewing PLWHA, based on a questionnaire that was pre-tested before the survey. The survey team was made of two people namely the investigator and the guide. This guide being himself a PLWHA, was used to direct the investigator to the addresses of PLWHA. The maximum duration of the questionnaire administration was 30 minutes, the maximum number of interviews per day was 11. Thus, data collection took 26 days to collect data to reach the target population (280 PLWHA).

2.6. Data analysis

All data were checked for quality control in order to identify records with inconsistencies and missing data. Different responses were coded into categories to make the analysis easy. The data were entered into Epidata 3.1. software and exported to SPSS version 20 for analysis. The frequencies of different variables (age groups, gender, occupation, education level, marital status, religion and economic level) were presented.

Descriptive measures such as mean and median were presented for the quantitative variables such as respondent age and treatment duration. In order to identify the determinants, it was carried out by the bivariate analysis (Chi-square test) and the calculation of Odds-Ratio and the confidence interval.

2.7. Ethical consideration

The research protocol for this study was submitted for approval to the ethical committee of Public Health School of Kinshasa. After being accepted by the above committee, we were allowed to start data collection. Each study participant had clearly and in writing expressed their consent to participate or not in the study, in accordance with the template. The confidentiality had been guaranteed by the use of a single investigator who had previously been trained in the PLWHA's CEP and the latter had been reassured of confidentiality; the anonymity of the information collected reinforced this confidentiality.

Apart from the time lost during the interview, this study did not cause any other risks for the respondents. The respondents did not have a direct benefit at the end of the interview, but indirectly this study made it possible to identify ways of improving the quality of PEC for PLWHA who took part in the survey. All cards were returned and filed in a locked cabinet, and access to the computerized database is locked, as only the principal investigator holds the code.

3. Results

3.1. Socio-demographic characteristics of respondents

The distribution of respondents following their socio-demographic characteristics is presented in the table below.

Table 1. Distribution of PLWHA under ART at the General Referral Hospital of Gbado-lite

| Variables | Frequency (n=280) | Percentage |
|--------------------|-------------------|------------|
| Sex | | |
| Male | 113 | 40.4 |
| Female | 167 | 59.6 |
| Age (years) | | |
| <25 | 5 | 1.8 |
| 25 – 34 | 79 | 28.0 |

| | | |
|-----------------------------|------------|------------|
| 35 – 44 | 146 | 52.1 |
| 45 and more | 50 | 17.9 |
| Marital status | | |
| Married | 124 | 44.3 |
| Uncommon relationship | 17 | 6.1 |
| Single | 17 | 6.1 |
| Divorced | 38 | 13.6 |
| Widow | 84 | 30.0 |
| Level of education | | |
| Illiterate | 16 | 5.7 |
| Primary | 79 | 28.2 |
| Secondary | 178 | 63.6 |
| University | 7 | 2.5 |
| Religion | | |
| Catholic | 80 | 28.6 |
| Protestant | 75 | 26.8 |
| Kimbanguist | 7 | 2.5 |
| Islam | 5 | 1.8 |
| Armée du salut | 1 | 0.4 |
| Revival church | 112 | 40.0 |
| Occupation | | |
| Civil servants | 43 | 15.4 |
| Traders | 35 | 12.5 |
| Student | 8 | 2.9 |
| Taximans (Tolekist) | 10 | 3.6 |
| Housewife | 17 | 6.1 |
| Farmer | 51 | 18.2 |
| Soldier | 10 | 3.6 |
| Jobless | 106 | 37.9 |
| Socio-economic level | | |
| Low level | 244 | 87.1 |
| High level | 36 | 12.9 |
| Total | 280 | 100 |

More than the half of people under ART at GRH of Gbado-lite are female (59.6%), the range age which is the most represented is between 35 and 44 years (52.1%). As for the marital status, married was the most represented group (44.3%) while most of them had a secondary level (63.6%), praying at revival church (40%) and are from household having a low income (87.3%).

The distribution of respondents following the characteristics related to the treatment is presented in table 2 below.

Table 2: Distribution of PLWHA under ART at GRH of Gbado-lite in 2017 following the characteristics related to the treatment

| Variables | Frequency (n=280) | Percentage |
|---|-------------------|------------|
| Type of drug combination | | |
| AZT+3TC+NVP | 78 | 27.9 |
| TDF+3TC+EFV | 202 | 72.1 |
| Duration of ART (months) | | |
| ≤ 60 months | 213 | 76.1 |
| > 60 months | 67 | 23.9 |
| Modification of therapeutic scheme | | |
| Yes | 109 | 38.9 |
| No | 171 | 71.1 |
| Not taking drugs for two days | | |
| Yes | 143 | 51.1 |

| | | |
|--|------------|------------|
| No | 119 | 42.5 |
| Resort to other treatments than ART | | |
| Yes | 33 | 11.9 |
| No | 247 | 88.1 |
| Knowledge on ART principles | | |
| Low level of knowledge | 170 | 60.7 |
| High level of knowledge | 110 | 38.3 |
| Total | 280 | 100 |

As observed above, 72.1% of respondents are under the combination of TDF+3TC+EFV while 76.1% spent more less five years under ART. Moreover, 38.9% of respondents recognized that their treatment have been once modified. More than the half (51.1%) declare having spent more than two days without the drug administration while 11.9% have resorted to other treatments.

Table 3 presents the distribution of PLWHA at Gbado-lite GRH following the appreciation of PEC structure.

Table 3: Distribution of PLWHA according to their appreciation of PEC structure

| Variables | Frequency (n=280) | Percentage |
|---|--------------------------|-------------------|
| Distance between the GRH and the house of PLWHA | | |
| ≤10 Km | 165 | 58.9 |
| >10 Km | 115 | 41.1 |
| Spending of money for transport | | |
| Yes | 119 | 42.7 |
| No | 161 | 57.3 |
| Continuation of treatment at GRH of Gbado-lite | | |
| Yes | 173 | 61.8 |
| No | 107 | 38.2 |
| Continuation of treatment with the same responsible of CDV | | |
| Yes | 277 | 98.9 |
| No | 3 | 1.1 |
| Total | 280 | 100 |

Among the PLWHA surveyed, 41% of respondents cover more than 10 km of walk from the GRH of Gbado-lite whose some respondents were covering 100 Km from the hospital. Concerning the supplies of medication, 42.7% of respondents declare spending money for the transport in order to reach the hospital setting to get new supplies of drugs. While 38,2% recognize not continuing the treatment due to the long distance separating them from the hospital. As per the care service, 98.9% of PLWHA have declared to trust the caregiver of this hospital.

The distribution of PLWHA according to socio-cultural environment characteristics is presented in the table below.

Table 4 : Distribution of PLWHA following the characteristics of their socio-cultural environment

| Variables | Frequency | Percentage |
|--|------------------|-------------------|
| Sharing of serological statu with peers | | |
| Yes | 228 | 81.4 |
| No | 52 | 18.6 |
| Supporting Association of PLWHA | | |
| Yes | 48 | 17.1 |
| No | 232 | 82.9 |
| Membership to PLWHA association | | |
| Yes | 117 | 41.8 |
| No | 163 | 58.2 |

| | | |
|---------------------------------------|-----|------|
| Fear of stigmatisation | | |
| Yes | 204 | 72.9 |
| No | 76 | 27.1 |
| Support of community mediators | | |
| Yes | 0 | 0.0 |
| No | 280 | 100 |

It is observed that 81.4% of PLWHA interviewed had shared their HIV status with other family members; 82.9% do not receive support from PLWHA support associations. While 41.8% belonged to a PLWHA association and 72.9% are afraid of stigmatization. None of them had benefited from the visits of the community mediators for any reason whatsoever. The mean age of PLWHA surveyed was 38.7 ± 7.2 years.

3.2. Prevalence of the non compliance

Figure 1 below gives the prevalence of non-compliance to ART.

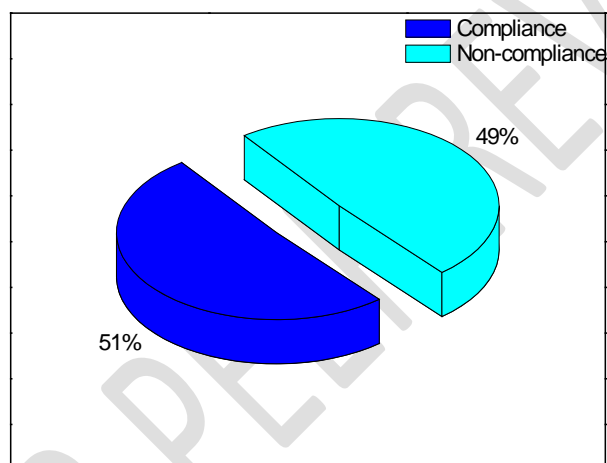


Figure 1: Frequency of non-compliance to ART among PLWHA at GRH of Gbado-lite

It was observed that the non compliance for the treatment was of 51% with CI at 95% (45.0 – 56.8).

Different reasons mentioned for the non-compliance of ART are given in the figure below.

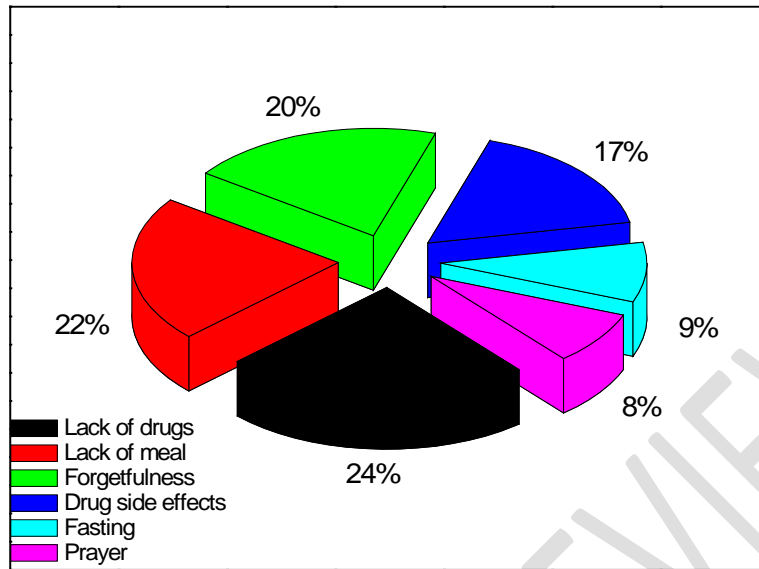


Figure 2: Diagram of the proportions of reasons for non-compliance

Among the PLWHA followed at the GRH in Gbadolite, 143 were non-compliant during the month preceding the survey (51.1%). The reasons for this non-compliance are drug discontinuation (24.4%), lack of meal (21.6%), forgetfulness (20.0%); drug side effects (16.9%), fasting (8.7%) and travel (8.4%).

3.3. Bivariate analysis

The socio-demographic and economic determinants of non-compliance of ART treatment is presented in the table below.

Table 5. Socio-demographic and economic determinants of non-compliance of ART treatment

| Variables | Modalities | Non-compliance | | OR (CI à 95%) | p-value |
|--|--------------------|----------------|-------------|---------------|---------|
| | | Yes | No | | |
| Sex | Female | 94 (56.3%) | 73 (43.7%) | 1.655 | 0.04 |
| | Male | 49 (43.8%) | 63 (56.2%) | | |
| Not taking medication for religious reasons | Yes | 26 (83.9%) | 5 (16.6%) | 5.822 | 0.000 |
| | No | 117 (47.2%) | 131 (52.8%) | | |
| Education level | Low | 64 (67.4%) | 31 (32.6%) | 2.770 | 0.000 |
| | High | 79 (42.7%) | 106 (57.3%) | | |
| Marital status | Single | 115 (82.7%) | 24 (17.3%) | 4.642 | 0.000 |
| | In a relationship | 28 (19.9%) | 113 (80.1%) | | |
| Profession | With occupation | 82 (47.4%) | 91 (52.6%) | | |
| | Without occupation | 61 (57.0%) | 46 (43.0%) | | |
| Income level | Low | 132 (54.1%) | 112 (45.9%) | 2.679 | 0.008 |
| | High | 11 (30.6%) | 25 (69.4%) | | |

Factors associated with the non-compliance to ART amongst PLWHA at the GRH of Gbado-lite are : Female ($p=0,040$; $OR=1,655$; $CI (1,023 - 1,704)$) ; religion : revival churches ($p=0,000$; $OR=5,867$; $CI (2,182 - 15,772)$) ; the low education level ($p=0,000$; $OR=2,770$ avec $CI (1,649 - 4,652)$) ; the low socio-economic level ($p=0,008$; $OR=2,679$; $CI (1,262 - 5,685)$) and being single ($p=0,000$; $OR=4,642$; $CI (3,196 - 6,840)$).

The drug determinants of non-compliance to ART is described in the table below.

Table 6. Drug determinants of non-compliance to ART

| Variables | Modalities | Non-compliance | | OR (CI 95%) | p-value |
|--|--------------------------------------|----------------|-------------|-------------|---------|
| | | Yes | No | | |
| Lack of knowledge on the duration of treatment | Yes | 106 (55,5%) | 86 (44,5%) | 1,699 | 0,041 |
| | No | 37 (42,0%) | 51 (58,0%) | | |
| | Low level | 103 (60,6%) | 67 (39,4%) | | |
| Knowledge of ART | High level | 40 (36,7%) | 69 (63,3%) | | |
| | AZT+3TC+NVP | 41 (52,6%) | 37 (47,4%) | | |
| Type of combination | TDF+3TC+EFV | 02 (50,7%) | 99 (49,3%) | | |
| | Modification de schéma de traitement | Yes | 72 (64,3%) | 40 (35,7%) | 2,434 |
| Durée passée sous TARV | No | 71 (42,5%) | 96 (57,5%) | | |
| | >60 months | 45 (68,7%) | 21 (31,3%) | 1,738 | 0,001 |
| Number of ART medication each day | ≤60 months | 97 (45,5%) | 116 (54,5%) | | |
| | 1 administration | 98 (51,3%) | 93 (48,7%) | | |
| Number of tablets taken per day | 2 administrations | 45 (50,6%) | 44 (49,4%) | | |
| | 1 tablet | 105 (50,5%) | 103 (49,5%) | | |
| Resort to other treatments | 2 tablets | 38 (52,3%) | 34 (47,2%) | | |
| | Yes | 20 (60,6%) | 13 (39,4%) | | |
| | No | 123 (50,0%) | 123 (50,0%) | | |

For the treatment risk factors, the lack of knowledge about the duration of ART by PLWHA was associated with non-compliance ($p=0.041$; $OR=1.699$; $CI (1.020 - 2.829)$); the low level of knowledge about ART principles was also associated with $p=0.000$; $OR=2.652$, $IC (1.614 - 4.356)$; the duration of more than 5 years on ART was also associated with the non-compliance ($p=0.001$; $OR=1.738$; $IC (1.197 - 2.528)$) and the modification of treatment regimen, with $p=0.000$, $OR=2.434$ and $CI (1.486 - 3.987)$. There was no association between type of combination therapy, number of tablets taken per day and the non-compliance. The same applies to the use of traditional treatment.

Structural determinants of non-compliance with ART treatment is presented in the table below.

Table 7: Structural determinants of non-compliance with ARV treatment among PLWHA visiting GRH

| Variables | Modalities | Non-compliance | | OR (CI à 95%) | p-value |
|---|------------|----------------|-------------|---------------|---------|
| | | Yes | No | | |
| Distance between HRG and the residence of PLWHA | ≤10 Km | 48 (42.1%) | 66 (57.9%) | 1.840 | 0.013 |
| | >10 Km | 95 (57.2%) | 71(42.8%) | | |
| To be out of ART at HRG | Yes | 43 (59.7%) | 29 (40.3%) | | |
| | No | 100(48.1%) | 108 (51.9%) | | |
| Confidence in caregivers | Yes | 140 (50.5%) | 137 (49.5%) | | |
| | No | 3 (100%) | 0 (0.0%) | | |
| Monitoring of treatment in the same health facility | Yes | 45 (42.1%) | 62 (57.9%) | 1.800 | 0.018 |
| | No | 98 (56.6%) | 75 (43.4%) | | |

This table shows that the distance of more than 10 km between the residence of PLWHA and the HGR (physical inaccessibility of the HGR) was associated with the non-compliance with $p=0.013$; OR=1.840 ; CI (1.136 - 2.981). PLWHA's refusal to continue the treatment in the same health facility was associated with the non-compliance with $p=0.018$; OR=1.800 and CI (1.106 - 2.932). There was no association between variables related to the patient-caregiver relationship and non-compliance.

Table 8 describes the socio-cultural determinants of non-compliance with ART among PLWHAs.

Table 8: Socio-cultural determinants of non-compliance with ARV treatment among PLWHAs

| Variables | Modalities | Non-compliance | | OR (CI à 95%) | p-value |
|--|------------|----------------|-------------|---------------|---------|
| | | Yes | No | | |
| Sharing one's serological status with siblings | Yes | 115 (50.7%) | 112 (49.3%) | | |
| | No | 28 (53.8%) | 24 (46.2%) | | |
| Not being a member of PLWHA association | Yes | 21 (72.4%) | 8 (27.6%) | 2.776 | 0.015 |
| | No | 122 (48.6%) | 129 (51.4%) | | |
| Support of associations to PLWHA | Yes | 14 (82.4%) | 3 (17.6%) | 4.811 | 0.008 |
| | No | 129 (49.2%) | 133 (50.9%) | | |
| Fear of stigmatization | Yes | 89 (43.6%) | 115 (56.4%) | 1.947 | 0.000 |
| | No | 54 (71.1%) | 137 (48.9%) | | |

In this table, it emerges that the lack of support from associations for PLWHA, the non-membership of the PLWHA association and fear of stigmatization were associated with the non-compliance with ART ($p=0.008$; OR=4.811; IC (1.351 - 17.137). $P=0.000$; OR=1.947; CI (1.291 - 2.986) and $p=0.015$; OR=2.776 and IC (1.185 - 2.501). No association with shared HIV status.

Determinants of non-compliance with ART among PLWHA is presented in the table below.

Table 9: Determinants of non-compliance with ART treatment among PLWHA

| Variables | Non-compliance | | OR (CI à 95%) | p-value |
|---|----------------|--------------|-----------------------|---------|
| | Yes | No | | |
| Lack of knowledge on the treatment duration | 84 (44.5%) | 106 (55.5%) | 1.7 (1.020 – 2.829) | 0.021 |
| Low level of knowledge on ART | 67 (39.4%) | 103 (60.6%) | 1.4 (1.169 – 2.735) | 0.005 |
| Lonely life in ones marital status | 24 (17.3%) | 115 (82.7 %) | 18.6 (8.926 – 38.574) | 0.000 |
| Religion (revival church) | 5 (16.1%) | 26 (83.9%) | 9.2 (2.245 – 37.449) | 0.002 |

The table of the multivariate analysis according to the logistic regression model shows that there is a significant association between the lack of knowledge of treatment duration ($p=0.021$; $OR=1.7$ and $CI (1.020 - 2.829)$); the low level of knowledge of ART principles ($p=0.005$; $OR=1.4$; $CI (1.169 - 2.735)$); life alone in marital status ($p=0.000$; $OR=18.6$ and $CI 8.926 - 38.574$) and church revival religion ($p=0.002$; $OR=9.2$; $CI (2.245-37.449)$) with non-compliance among PLWHA surveyed.

4. Discussion

4.1. Prevalence of the non-compliance

In this study, the compliance was measured based on PLWHA's reports of compliance with medication use during the month preceding the survey and on the count of the rest of the month's remaining tablets. Was considered non-compliant if any PLWHA had spent at least 2 days during the month without taking their medication; or if the number of tablets counted was higher than expected based on the number of days spent in the same month. Many authors are unanimous that no ideal measure instrument exists which allows to assess the compliance of real patients. To compensate for this deficit, they recommend crossing at least one objective method with a subjective method, in order to obtain a more accurate approximation of patient compliance. The prevalence of non-compliance observed in the study was 51.1%. Studies by other authors in Africa show that the prevalence of non-compliance varies from 27 to 65% [22, 26-29, 32]. In DRC Ngona found the prevalence of 40.2% in Bunia [33]. The 51.1% prevalence found in this work is similar to previous studies undertaken in Africa. For the evaluation timeframe, in a study of the cohort of patients followed in Dakar, this evaluation covered the last 30 days. Although some authors are aware that this approach can bring loss of information [35-36].

4.2 Reasons for non-compliance

The main reasons given by the respondents were drug discontinuation (24.4%), absence of meals (21.6%); forgetting (20.0%); side effects (16.9%); fasting (8.7%) and travel (8.4%). Essomba *et al.* found that the main causes of non-compliance were forgetfulness (32.9%), drug discontinuation (14.0%) and occupations of daily living (12.8%) [36]. Meanwhile, Oumar *et al.* in order of frequency had found forgetting, daily living burdens, fatigue and drowsiness, work travel, negligence and ignorance that it is a long term treatment [32]. Other authors had reported differently the absence of meals, adverse drug reactions, drug discontinuation, geographical inaccessibility of CEP structure [26, 37-38]. Fasting was mentioned in these different studies.

4.3. Socio-demographic and economic determinants

The average age of the respondents was 38.7 ± 7.2 years. The most affected age group was 35-44 years while the minimum age was 19 and the maximum was 57. These findings are similar to those found by Guira *et al.* and Essomba *et al.* who found the same average age range in Burkina Faso and Cameroon in 2016 respectively. The most concerned age group was 30-44 years of age in Essomba's work [26, 36-38].

The sex ratio was 1.5 in favour of the female sex. Married couples accounted for 50.4% of the total and 49.6 lived alone (single, divorced and widowed people living alone). Saïdou in 2010 in the study of

antiretroviral treatment compliance at the NGO Wale de Ségou on 218 cases found that 56% of patients were in a conjugal union [39-40]. Mbopi-Kéou in a study of factors related to antiretroviral treatment compliance in Cameroon report the same findings regarding the proportion of PLWHA in a conjugal union [29, 37]. As for the level of education, 63.6% of respondents were at the secondary level.

4.4. Treatment regimen, duration of treatment and knowledge of ART principles

In relation to ART, two types of combinations were used, namely Zidovudine, Lamivudine and Nevirapine in 27.9% and Tenofovir, Lamivudine and Efavirenz in 72.1%. In terms of treatment duration, 76.1% had spent no more than 5 years on ART and 60.7% had a low level of knowledge of ART principles. The level of knowledge of ART varies in the literature. This variability results from the nature of the measured knowledge.

4.5. Characteristics of PLWHA by socio-cultural environment

In relation to the socio-cultural environment, 81.4% of respondents had informed at least one member of their family of their HIV status; 82.9% had never received associative support and 41.8% belonged to a PLWHA association while 72.9% were afraid of stigma. No patients had been visited by a social worker or community mediators as part of their treatment.

Kanté in 2011 found in his study on ART compliance in Mali a low rate of patient adherence to a PLWHA association, while 61.8% shared their HIV status with their relatives. In addition, Hachfi et al. In 2012, their study in Tunisia reported that a fraction of patients whose proportion was not specified were taking their medication in secret for fear of stigmatization [22, 28].

4.6. Characteristics of the respondents according to their views on the organization of the care institution

Speaking of the PEC structure which is the Gbadolite GRH, 41.1% of the respondents had experienced a problem of geographical inaccessibility of the HGR; 42.7% spent money on transport to reach the institution for appointments. 61.8% had stated that they wanted to continue treatment in the same HGR. 98% trusted the caregivers and all of them appreciated their attitude and welcome. Geographic inaccessibility had been highlighted by Fatoumata and Hachfi W. et al. as a factor in women's abandonment of ART in Guinea and Tunisia.

4.7 Factors Associated with Non-Compliance in Bi-variate Analysis

4.7.1. Varied uni analysis of the socio-demographic characteristics of the respondents

Research has indeed shown significant variability in the socio-demographic characteristics associated with non-observance. This variability can be explained at s'expliquer d'une by differences in the populations studied, the sample size and d'autre by the method used in Essomba (2016). Kanté and Oumar et al. had not found an association between socio-demographic factors and non-observance [22, 32, 36].

In the present work, the female sex was associated with non-observance ($p=0.040$; $OR=1.655$; $IC (1.023 - 1.704)$); religion was also associated ($p=0.000$; $OR=5.867$; $IC (2.182 - 15.772)$). The work of M. Bastard et al. In Senegal, on the contrary, found that the female sex was associated with good compliance and that the male sex was a non-observance factor. The works consulted did not mention an association between religion and non-observance, except for the proportions of representativeness given by ISSA. Nevertheless, in her work in France, Pasquier had identified religion as a factor of non-observance of ART in a woman of African origin [31, 38, 42].

With revival churches promising miraculous healings to followers, religion is gradually becoming a factor influencing ART. Patients are afraid to take their medications during the young prayer period fearing the adverse effects of fasting on these antiretroviral molecules. The low level of education associated with non-observance ($p=0.000$; $OR=2.770$ with $CI (1.649 - 4.652)$) This result is similar to those observed by Hachfi, 2012 in Tunisia and Oumar in Mali. The high level of education allows patients to understand and maintain ART instructions

The low socio-economic level associated with ($p=0.008$; $OR=2.679$; $CI (1.262 - 5.685)$). This could be explained by the fact that PLWHA who had a low socio-economic level were in the majority among the respondents, representing 87.1%. On the other hand, the work of Wilson E. et al. and Boubou Kanté did not mention a clear association between the low socio-economic level but indicated that 16% and 34% of patients respectively had financial difficulties in accessing PEC structures and were therefore non-observers [22, 43]. The bachelor life in marital status was associated with non-observance with ($p=0.000$; $OR=4.642$; $IC (3.196 - 6.840)$). This result is consistent with those obtained by ISSA in a study of ART compliance among patients followed at the GAO hospital in 2008 and Kanté in 2011 found that married couples are more observant than single and widowed people [22, 38]. But Gervais had found the opposite in his work: the determinants of non-compliance with antiretroviral therapy by adult HIV-infected patients and follow-up at the Cotonou NHRC in 2003 [44]. The occupation (profession) of PLWHA was not associated with non-observance.

4.5.2. Analysis of processing factors

For treatment risk factors, lack of knowledge about the duration of ART by PLWHA was associated with non-compliance ($p=0.041$; $OR=1.699$; $CI (1.020 - 2.829)$); low level of knowledge about ART principles was also associated with $p=0.000$; $OR=2.652$, $IC (1.614 - 4.356)$; duration of more than 5 years on ART was also associated with non-compliance ($p=0.001$; $OR=1.738$; $IC (1.197 - 2.528)$) and modification of treatment regimen, with $p=0.000$, $OR=2.434$ and $CI (1.486 - 3.987)$. Kanté and Oumar had found an association between insufficient knowledge of ART and the use of traditional treatment with non-compliance. The association between modification of therapeutic combination and non-observance. E. Essomba had found the association of treatment modification with non-compliance but was not significant [22, 32, 36].

In this work There was no association between the type of therapeutic combination, the number of tablets taken per day and non-compliance. The same applies to the use of traditional treatment. This was not the case with Mbopi-Kéou who found that the use of other treatments during ART was associated with non-compliance. As for the duration spent on ART, Mbopi-Kéou and Gervais F. had found results contrary to what is found in this work; they had found that compliance improves with the duration of ART, while the duration of more than 5 years spent on ART was associated with non-observance. Patients who had spent more than 5 years on ART relied on their treatment experience and occasionally had treatment neglect. Gervais F had also found that the change in prescription was significantly associated with non-compliance [29, 44].

4.5.3. Analysis of factors associated with the organization of the PEC structure

The analysis table shows that the distance of more than 10 km between the residence of PLWHA and the HGR (inaccessibility of the HGR) was associated with non-observance with $p=0.013$; $OR=1.840$; $CI (1.136 - 2.981)$. PLWHA's Refusal to continue treatment in the same HGR was associated with non-compliance with $p=0.018$; $OR=1.800$ and $CI (1.106 - 2.932)$. There was no association between variables related to the patient-caregiver relationship and non-compliance.

The geographical inaccessibility of the Gbadolite HGR was associated with non-compliance among PLWHA. The 41.1% of PLWHA living more than 10 km from the HGR had accused the inaccessibility of this PEC institution. Some were more than 200 km from the Gbadolite HGR; had even declared that they no longer wanted to continue treatment in the Gbadolite HGR because they were very far from their place of residence. Hachfi et al. and Oumar found geographic inaccessibility as a factor associated with ART non-compliance [27-28].

4.5.4. Analysis of factors related to the socio-cultural environment

The analysis shows that the lack of support from associations for PLWHA, fear of stigmatization and non-participation in PLWHA association were associated with non-observance of ART with respective values of $p=0.008$; $OR=4.811$; $CI (1.351 - 17.137)$. $P=0.000$; $OR=1.947$; $CI (1.291 - 2.986)$ and $p=0.015$; $OR=2.776$ and $CI (1.185 - 2.501)$. No association with shared HIV status.

Sharing serological status with relatives was found by Oumar et al. as a factor of good compliance; Kanté and Gervais had found that patients whose immediate family and friends were not informed of their treatment were significantly more unobservant with ART [22, 27, 44]. Fear of stigmatization drove the

Tunisian patients on whom Hachfi et al. had worked to take the drugs in secret, making them non-compliant with ART [28]. Non-membership of a PLWHA association was significantly associated with non-adherence to ART among patients in the Yuliana Health District in Mali. 41.9% of PLWHA who belonged to the PLWHA association reported that the association allowed them to accept and live with the disease. It constituted (the association) a place of moral and psychological support [22].

4.6. Factors associated with non-observance in multi-varied analysis

The table of the multi-varied analysis according to the logistic regression model above shows that it had a significant association between lack of knowledge of treatment duration ($p=0.021$; OR=1.7 and CI (1.020 - 2.829)); the low level of knowledge of ART principles ($p=0.005$; OR=1.4; CI (1.169 - 2.735)); life alone in marital status ($p=0.000$; OR=18.6 and CI 8.926 - 38.574)) and church revival religion ($p=0.002$; OR=9.2; CI (2.245 - 37.449)) with non-compliance among PLWHA surveyed. People who did not know that ARV treatment was for life, who had insufficient knowledge about ARV drugs, who were single, divorced or widowed and who prayed in the revival churches were more likely to not adhere to their treatment than others. Knowledge is necessary for good compliance as it allows patients to behave in ways that contribute to the effectiveness of ART. Lack of or insufficient knowledge of ART was identified by many authors as a factor associated with poor ART compliance [22, 32]. As for marital status, the authors had found the association in either direction. The result of this work corroborates those obtained by Issoufi in a study of ART compliance of patients followed at the GAO hospital in 2008 and Kanté in 2011 found that married couples are more observant than single and widowed people; but Gervais F found the opposite [22, 38, 44].

Religion had hardly been cited as a factor of non-observance of ART in the literature we consulted. Nevertheless, Pasquier et al. in France had reported non-observance by a woman of African origin linked to her religious belief [42]. With revival churches promising miraculous healings to followers, religion is gradually becoming a factor influencing adherence to ART. Patients are afraid to take their medications during the young prayer period fearing the adverse effects of fasting on these antiretroviral molecules.

4.10. Limitations of the study

Because of its cross-sectional nature, this study has limitations in terms of the certainty of the association between non-compliance and the factors identified above. Only a longitudinal cohort study can determine this association with certainty. This study has another limitation with respect to the compliance measurement technique. Many authors prefer to measure compliance over the last 4 to 7 days before the survey. For this study, compliance was measured over the 30 days prior to the survey. Finally, for the measurement of ART knowledge, questions related to past realities may be subject to recall bias, which was evident to some PLWHA who had difficulty remembering instructions about ART received from health workers.

CONCLUSION

ART is currently one of the key areas in the fight against HIV infection. Its effectiveness is due to strict compliance. This study, which aimed to determine the factors associated with ART non-observance in patients followed at HGR Gbadolite, showed that the prevalence of non-observance remains high in these patients. Non-compliance was significantly associated with insufficient knowledge of treatment by these patients, marital status and religion, mainly revival churches. Nevertheless, the geographical inaccessibility of Gbadolite's HGR remains a real concern for the patients who are treated there. The results obtained suggest the need to consider the barriers related to the factors identified in the treatment adherence process. In light of these factors, this study provides the basis for a reflection on the need to improve communication strategies in pre-therapeutic and adherence consultations in order to reduce the risk of non-compliance.

This work lays the foundation for further research that could, in order to understand compliance more fully, focus on other patients followed in other hospitals in Nord Ubangi province in order to strengthen the fight against AIDS in this new province.

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