Determinants of adherence to antiretroviral therapy in people living with HIV, followed up at Lubumbashi, Democratic Republic of Congo

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ABSTRACT

Aims: The aim of the present study was to determine the level of adherence and the factors associated with good adherence to antiretroviral treatment (ART) among people living with HIV (PLHIV).

Study design: Cross Sectional Study
Place and Duration of Study: Internal medicine department (Infectious Diseases Unit), Lubumbashi University Clinics, in Democratic Republic of Congo (DRC), between 15th May 2021 and 17th July 2021.
Methodology: We included 137 patients (56men, 81 women; age range 18-70 years) with HIV and,all participants were interviewed on a first-come, first-served basis.The association between factors affecting adherence and the level of adherence was analyzed using a multiple logistic regression model, and odds ratios (ORs) with 95% confidence intervals (CIs) calculated.Among 137 PLHIV, 76.64% had good ART adherence (≥95%). Bivariate analysis revealed numerous factors associated with adherence (P = 0.05). However, in multivariate analysis, being on ART for more than three years and abstinence from alcohol were the factors influencing good ART adherence (P = 0.05).
Results: Among 137 PLHIV, 76.64% had good ART adherence (≥95%). Bivariate analysis revealed numerous factors associated with adherence (*P* = .05). However, in multivariate analysis, being on ART for more than three years and abstinence from alcohol were the factors influencing good ART adherence (*P* = .05).
Conclusion: Raising awareness among PLHIV, regular counseling of patients regarding daily intake of antiretroviral drugs and abstinence from alcohol, could contribute to good adherence and long-term success of ART among PLHIV.

Keywords: ART, HIV/AIDS, adherence, DRC

1. INTRODUCTION

The World Health Organization (WHO) currently estimates that 37.7 million (30.2 million-45.1 million) people were living with the human immunodeficiency virus (HIV) in 2020, of whom 680,000 (480,000-1.0 million) died of AIDS-related illnesses and around 1.5 million [1.0 million-2.0 million] became newly infected with HIV by the end of 2020 [1].
WHO also reports that only 28.2 million people living with HIV had access to antiretroviral treatment by June 30, 2021 [1,2].
Although the introduction of antiretroviral therapy (ART) has significantly reduced HIV-related morbidity and mortality in both developed and developing countries, sub-Saharan

Africa remains the epicenter of HIV, accounting for over 67% of the 37.7 million people living with HIV worldwide [1,3].

In line with the 95-95-95 goal of accelerating the response to HIV/AIDS (Acquired Immune Deficiency Syndrome) to end the HIV/AIDS epidemic by 2030, WHO has made everyone with HIV eligible for treatment, including pregnant women and children regardless of CD4 count, "treating everyone" [4,5].

In the Democratic Republic of Congo (DRC), the 2018-2019 national HIV/AIDS response report, indicates that around 527,831 people are living with HIV/AIDS, representing a prevalence of 0.8%. 321,222 (60.8%) people are on antiretroviral treatment, 51% of whom had an undetectable viral load at the end of 2019 [6]. This situation suggests that the DRC has not been able to achieve the 90-90-90 targets, which stipulates that by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people diagnosed with HIV infection will receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have viral suppression [4].

Antiretroviral drugs are the therapeutic mainstay in the control and prevention of infection caused by the Human Immunodeficiency Virus (HIV). The current antiretroviral regimens include drugs with impressive inhibitory power on viral replication, thus reducing viral load to an undetectable level, improving the quality of life of people living with HIV and helping to reduce HIV-related morbidity and mortality [3,7].

Antiretroviral treatment does not cure HIV infection, but it can control disease progression and effectively suppress viral replication when taken at the right time, in an optimal manner. It also prevents the onset and progression of opportunistic infections by increasing CD4 counts [10,11].

However, the efficacy of these antiretroviral drugs depends mainly on patient adherence to treatment [8,9]. Medication adherence is defined by WHO as "the extent to which a person's behavior with regard to taking medication, following a diet and/or making lifestyle changes corresponds to the agreed recommendations of a healthcare provider" [4].

Treatment adherence and medication compliance are necessary for HIV-infected patients to optimize ART efficacy. Getting patients to take medication daily is one of the greatest challenges for effective antiretroviral therapy, as poor adherence to treatment can lead to virological failure and drug resistance [16].

The extent and impact of poor adherence to antiretroviral drugs is greater in developing than in developed countries [11]. For instance, in an Ivorian study carried out at the Wale medical-social center in Yamoussoukro, Indri-Kouakou found an antiretroviral (ARV) adherence rate of 77.8% for men and 79.8% for women [12]. In Nepal, at the Chitwan antiretroviral treatment center, Sujan Neupane et al found an overall ARV adherence rate of 87.4% [2].

To determine the true level of ARV adherence, data is needed in developing countries among people living with HIV such as adults, adolescents, children and pregnant women, marginal and key populations. Many previous studies in our setting have focused solely on the epidemiological aspect, and very few have explored ART adherence levels. Yet the key to the success of antiretroviral treatment programs and the prevention of treatment failure lies in consistently high levels of adherence.

The present study aims to determine the level of adherence to antiretroviral drugs and its associated factors among PLVIH receiving antiretroviral therapy in a university hospital in the south of the Democratic Republic of Congo.

2. MATERIAL AND METHODS

2.1. Study design and context

A descriptive cross-sectional study was carried out in a tertiary care teaching hospital in the south of the Democratic Republic of Congo (CliniquesUniversitaires de Lubumbashi) between 15th May 2021 and 17th July 2021. The CliniquesUniversitaires de Lubumbashi has a care unit for patients (adults and children) suffering from HIV/AIDS. The unit currently has a cohort of 3855 HIV patients (including satellite centers). All these patients are on antiretroviral therapy (ART).

The first-line regimen used in the DRC since 2018 is as follows: TDF (300 mg)/ 3TC (300 mg) /DTG (50 mg); The second-line regimen is TDF (300 mg) / 3TC (300 mg) / EFV (400 mg) [6].

All patients attending the PLHIV care unit at Lubumbashi University Clinics were considered the sample population. Inclusion criteria were patients aged ≥18 years, on antiretroviral therapy (ART) for at least six months and attending the hospital during the data collection period.

Notwithstanding, patients reluctant to participate in the study and patients with known hearing impairment and mental disorders were excluded from the study.

2.2. Determination of sample size and sampling procedure

Participants were selected using the systematic random sampling method, and all 137 participants were interviewed on a first-come, first-served basis.

The sample was determined by.

$$n = \frac{NZ^2p(1\text{-}P)}{d^2(N-1)+Z^2p(1\text{-}P)}$$

z_α = 1.96 for 95% confidence interval.
p = Prevalence of ART Adherence.
(p = 0.7)
d = precision or error in the study = 0.02.
Total eligible study population were (N) =150.

Sample size =142 + 10% non response rate.
= 157.

2.3. Data collection tool and procedure

A structured, interviewer-administered questionnaire was used to collect data in a face-to-face interview to assess treatment adherence over the last 1 month. Questions on explanatory variables were prepared using the WHO conceptual model and by reviewing the international literature. A personal interview was conducted with each eligible study patient who met the inclusion criteria, and informed consent was obtained after explaining the interest of this study in some official and national languages (French, Swahili, and Lingala).

Pill counting is cost-effective, simple and more accurate than other methods [17]; however, the number of pills left does not necessarily reflect consistent medication use. Therefore, adherence status was assessed on the basis of the number of pills reported as actually taken one month prior to the data collection period, divided by the number of pills prescribed, multiplied by 100%. Patients who reported taking ≥95% of the prescribed medication were considered adherent (optimal); those reporting <95% uptake were classified as non-adherent (suboptimal).

Compliance was calculated using the following formula:

$$\text{Adherence percentage} = \frac{\text{Number of pills taken during the specific period (1month)}}{}*100$$

Number of pills to be taken during that specific period (1 month)

The compliance performance chart has been used to classify optimal and suboptimal compliance [2].

Table 1. Adherence performance chart

No of pills per day		Percentage of adherence		
		>95%	80-95%	<80%
1	Number of pills missed in a month	1	2 to 6	7 or more
2		3 or less	4 to 12	13 or more
3		4 or less	5 to 18	19 or more
4		6 or less	7 to 24	25 or more

2.4. Data management and analysis

Collected data were edited, coded and entered manually into Excel version 3.1 database software. The data was then exported to Statistical Package for Social (SPSS) version 25 for further statistical analysis.

In the bivariate analysis, the chi-square test and odds ratios were used to test the significance of the association between the independent variables and the dependent variable. Independent variables found to be significant at p-value 0.10 in the bivariate analysis were included in the multivariate logistic regression model. The multivariable logistic regression model was run to determine the net effect of independent variables on adherence to antiretroviral treatment.

A total of 137 cases were analyzed. Due to the presence of outliers, 5 cases were excluded from the analysis in order to adjust model fit. The goodness-of-fit of the model was assessed using the Hosmer and Lemshow test, which showed that the model was statistically insignificant.

Model adequacy was assessed by means of a scatter plot of the standardized residual, the value of leverage and Cooks' influence analogue.

3. RESULTS

3.1. Adherence rate

Of the 137 people surveyed, 76.64% were optimally adherent (took ≥95% of the prescribed medication).

The schematic representation of the adherence rate is shown in Fig. 1.

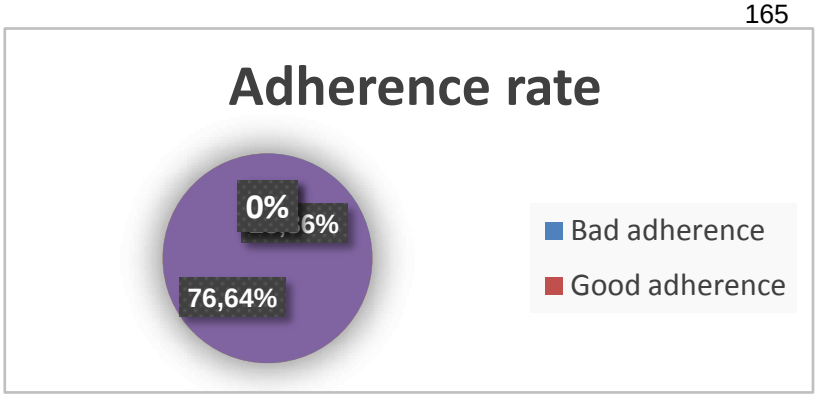

Fig.1. Level of adherence

3.2. Socio-demographic characteristics of respondents

Good adherence was observed in 76.64% of respondents. Females predominated (59.1%), and the average age of respondents was 41.8 years. The majority (70.1%) of patients belonged to the Protestant religion. 50.4% of respondents had a secondary education. Over 40.1% of the patients surveyed were married, while 34.3% were single. Most respondents did not consume alcohol (59.9%) or smoke cigarettes (88.3%). The majority of respondents were unemployed (55.5%); 52.6% had been on ARVs for less than three years and 47.4% for more than 3 years; 56.9% of respondents had not disclosed their HIV status to their close contacts, and 7.3% had a tuberculosis co-infection at the start of their ARV treatment.

Table 2. Baseline characteristics of the participants

Characteristics	Number	Percentage
Sex		
Feminine	81	59,1
Masculine	56	40,9
Ages (years)		
18- 29	20	14,6
30- 39	45	32,8
40- 49	37	27
≥ 50	35	25,5
Mean±SD	41,8±12,5	
Educationallevel		
Primary	29	21,2
Secondary	69	50,4
Tertiary	39	28,5
Marital Status		
Single	47	34,3
Married	55	40,1

Widow (widower)	23	16,8
Divorced	12	8,8

continued

Characteristics	**Number**	**Percentage**
Employment		
Employed	61	44,5
Non-employed	76	55,5
Alcoholconsumption		
Yes	55	40,1
No	82	59,9
Use of tobacco		
Yes	16	11,7
No	121	88,3
Co-infection TB/HIV		
Yes	10	7,3
No	127	92,7
Duration on ARV		
< 3 years	72	52,6
>3 years	65	47,4
Disclosure of HIV+ status		
Yes	59	43,1
No	78	56,9
Religion		
Catholic	39	28,5
Protestant	96	70,1
Muslim	2	1,5

3.3. Multivariable logistic regression model of factors associated with ART adherence

Using multivariable logistic regression of factors associated with ART adherence, respondents who did not consume alcohol were 5 times more likely to adhere to ART than those who did (OR= 5.36; CI: 1.94-14.79).

Participants aged 50 and over were 6 times more likely to adhere to ART than those aged under 50 (OR= 6.17; CI: 1.10-34.75).

Employed participants were 4 times more likely to adhere to ART than those who were unemployed (OR= 4.09; CI: 1.33-12.56).

The results of the multivariable logistic regression model of factors associated with ART adherence are presented in Table 3.

Table 3. multivariable logistic regression model of factors associated with ART adherence

Variables	Adherence optimal N(%)	Adherence sub optimal N(%)	P-value	OR(IC95%) Non adjusted	P-value	OR(IC95%) adjusted
Sex						
Female	60 (74,0)	21 (25,9)	0,54	1,35(0,63-2,86)		
Male	38 (67,8)	18 (32,1)		1		
Age (years)						
18- 29	10(50)	10(50)		1		
30- 39	29(64,4)	16(35,6)	0,17	2,4(0,8-7,3)	0,52	1,5(0,3-6,2)
40- 49	27(73)	10(27)	0,01	5,1(1,5-17,8)	0,09	3,7(0,7-18,3)
≥ 50	32(91,4)	3(8,6)	<0,00	10,6(2,4-46,5)	0,03	6,1(1,1-34,7)
Profession						
Employed	48 (78,6)	13 (21,3)	0,09	1,9(0,8-4,1)	0,01	4,0(1,3-12,5)
Non-employed	50 (65,7)	26 (34,2)		1		
Statut matrimonial						
Single	29(61,7)	18(38,3)		1		
Divorced	9(75)	3(25)	0,39	0,5(0,1-2,2)		
Widow	18(78,3)	5(21,7)	0,16	0,4(0,1-1,4)		
Married	42(76,4)	13(23,6)	0,10	0,4(0,2-1,1)		

Continued

Level of education						
Primary	19(65,5)	10(34,5)		1		
Secondary	49(71)	20(29)	0,58	0,7(0,3-1,9)		
Tertiary	30(76,9)	9(32,1)	0,29	0,5(0,1-1,6)		
Alcohol consumption	71(86,5)	11(13,4)	<0,0	6,6(2,9-15,2)	<0,0	5,3(1,9-14,7)
No	27(49,0)	28(50,9)	0	1	0	
Yes						
Use of tobacco						
No	92(76,0)	29(23,9)	0,00	5,2(1,7-15,8)	0,28	2,1(0,5-8,5)
Yes	6(37,5)	10(62,5)	1	1		
Duration on ARV						
<3years	41(56,9)	31(43,0)	<0,0	0,1(0,0-0,4)	0,42	0,6(0,1-1,9)
>3years	57(87,6)	8(12,3)	0	1		
Disclosure of HIV+ status	47 (79,7)	12 (20,3)	0,06	2,0(0,9-4,5)	0,38	0,6(0,2-1,7)
Yes	51 (65,4)	27 (34,6)		1		
No						
Religion						
Catholic	28(71,8)	11(28,2)	0,91	0,9(0,4-2,1)		
Protestant	68(70,8)	28(29,2)		1		
Muslim	2(100%)	0				

3.4. Model fit testing

Several standard measures of model fit were used to analyze model fit to observed data. Log-likelihood (LL) was used to access overall model fit. To see the degree of explanation by the covariates used in the model adjusted for variation in membership level, the pseudo R-two was calculated.

Negelkerke'spseudo R-two measures the proportion of variation in the dependent variables that can be explained by the model's predictors. Here, Rx2 =0.405, which means that 40.5% of the variation in adhesion rate was explained by the model's predictors (the independent variables.)

The results of the model fit test are presented in Table 4 (Table IV below).

Table 5. Model fit test

Model summary		
2 log likelihood	Cox et Snell R Square	Nagelkerke R Square
118,19	0,282	0,405
Hosmer et Lemeshow		
Chi carré	DL	Pvalue
4,269	8	0,832

3.5. Analysis for bias

Residuals were analyzed using the following graphs

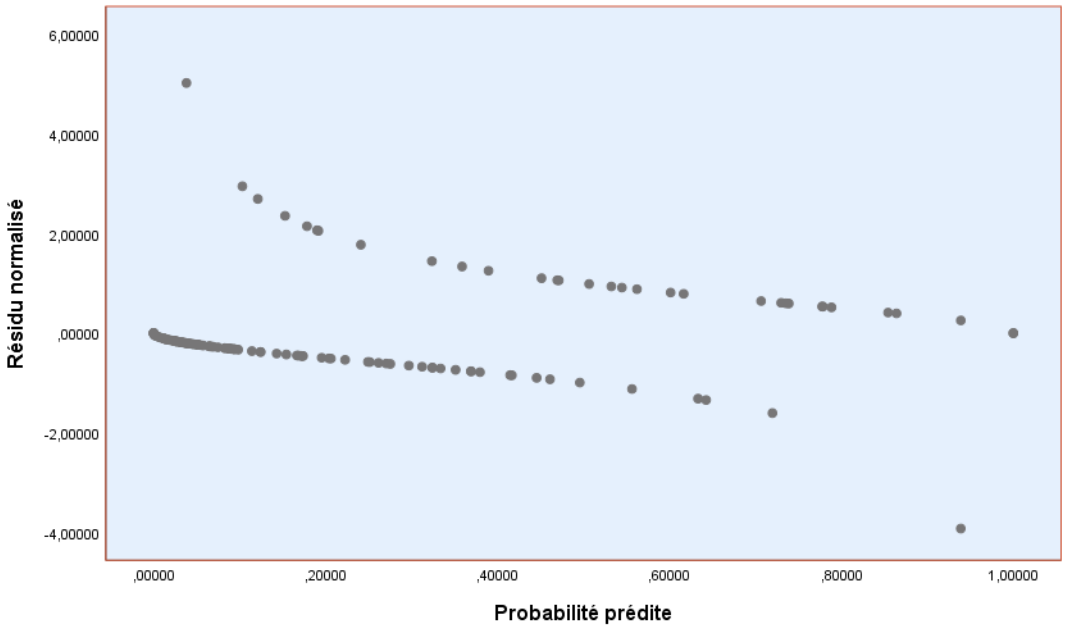

Fig 2: Scatter plot for outliers (standardized residual)

Standardized residuals for the adhesion level are shown in Fig. 2.

The figure shows that the standardized residual is less than 6, which means that there are no influential cases having an effect in the model.

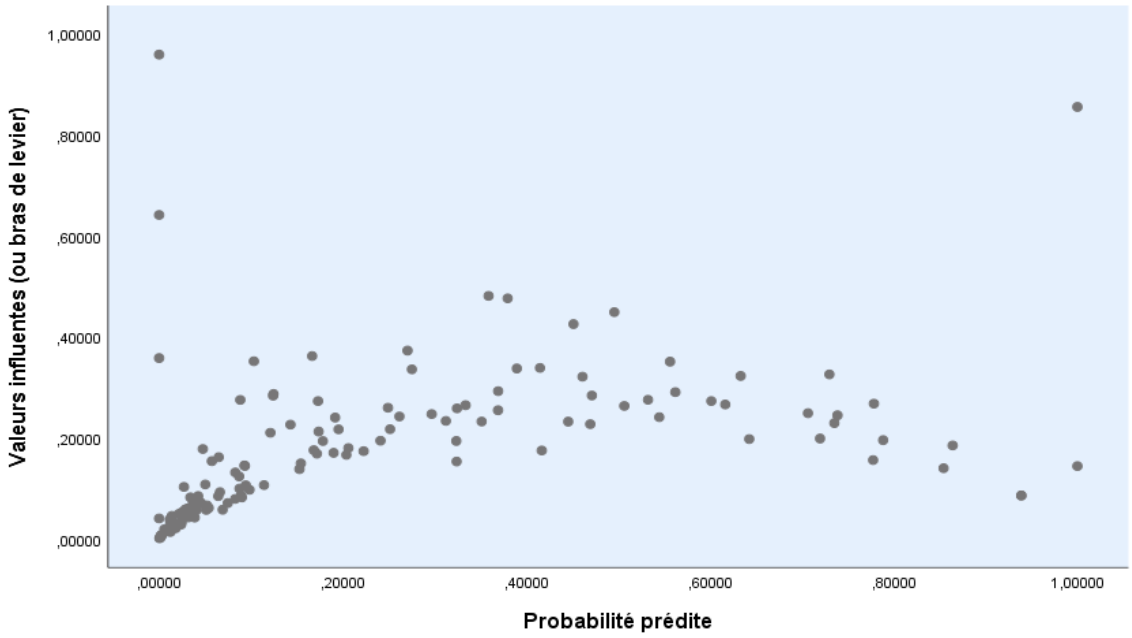

Fig 3. Scatter diagram for influential values (lever arm)

Another method of detecting influential values is the lever arm. According to the scatter plots of influential values for adhesion level, as shown in Fig. 3, influential values are below 0.6, indicating the absence of outliers.

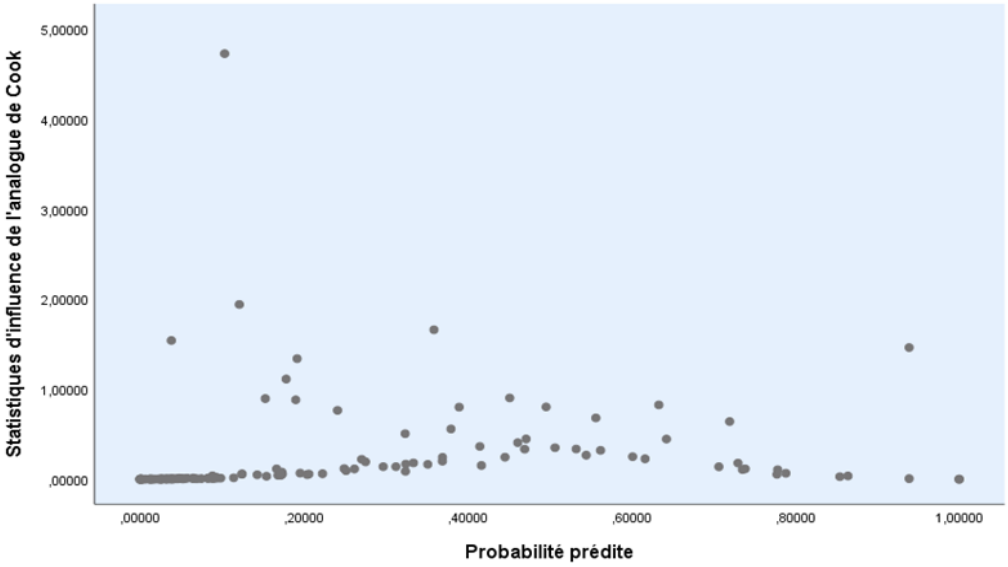

Fig 4. Scatterplots for outliers (Cooks influence analogue)

Cooks' distance is proposed to measure the effect of excluding a specific observation on the overall parameter estimates. Cooks gives the value of D, d > 1 identifies the case that could be influential, as shown in figure 4.

4. DISCUSSION

In this study, we examined the level of adherence to antiretroviral therapy and associated factors in PLHIV followed up in the care unit of the university clinic in Lubumbashi, DRC.

The results of our study indicate that, out of 137 PLHIV surveyed, 105 (76.64%) showed good adherence. The adherence rate in our setting was better than that found by Banagi et al in India (76.64% vs. 70.4%), and by Achappa et al [3,18-20]. However, other studies conducted in Nepal and Nigeria have shown better adherence to ART than the results of our study [2, 21].

The good level of adherence in our institution could be explained by the fact that the entire care team (doctors, nurses, peer educators) were involved in the follow-up of PLHIV receiving free ART. This follow up was conducted notably through pre-treatment counseling on the benefits of daily intake and the consequences of discontinuation or irregular intake of antiretroviral drugs (appearance of opportunistic infections and ART-resistant viral strains). The follow up also included telephone reminders, a few days before the ARV supply appointment.

This better adherence could also be due to the fear of stigmatization by society and redundance in their families,if the respondent's state of health should deteriorate. Therefore, they are obliged to adhere to treatment in order to maintain their social standing and fulfill their responsibilities in their families. Nevertheless, our results answered the research questions, an adherence rate to antiretroviral therapy of 76.64% was identified.

Pettersen et al found that patients did not adhere to their treatment regimen for reasons that could be intentional or unintentional [13]. Barriers to treatment adherence include fear of disclosure of HIV status, stigma, discrimination, forgetfulness and treatment discontinuation [3]. Medication-related factors may include adverse effects and complex dosing regimens. Health system factors include remoteness from health services, long waiting times for care, receiving only one month's worth of medication, pharmacy stock-outs and the burden of direct and indirect costs of care [4].

The chronicity of HIV and the duration of treatment also pose a significant threat to adherence. For instance, a study by Molloy et al highlighted a significant increase in the level of non-adherence to medication between the immediate treatment period and after six months of treatment [7]. Furthermore, The WHO has observed that patients with long-term illnesses have difficulty adhering to treatment instructions [8].

A study by Patou et al in Kinshasa (DRC) highlighted that food insecurity was significantly associated with non-adherence to ART. [14] He also discovered in a subsequent study that religious beliefs were both an obstacle and a facilitator to ART adherence [15].

In comparison with the studies mentioned above, the statistically significant determinants of adherence ($P<0.05$) in our study were non consumption of alcohol, age equal to or greater than 50 years and being employed.

Alcohol consumption has been incriminated in several studies as one of the main reasons for poor adherence to ART [2, 3, 19, 20]. In our study, participants who did not consume alcohol showed better adherence to ART compared with those who did, and this association between ART adherence and not consuming alcohol was statistically significant ($P< 0.05$). This could be due, on one hand, to the counseling initiated by healthcare providers prior to the start of ART, concerning the possible consequences of alcohol consumption on drug efficacy. It can also be assumed that participants who consumed alcohol regularly and got drunk, were more likely to forget to take their ARVs and therefore less adherent.

In our study, PLHIV aged over 50 years showed better adherence to ART than those aged less than 50 years ($P<0.005$). Our results are contrary to those found by Achhapa et al in India, who found that patients over 49 years of age were less adherent than patients under 49 years of age. The reasons being that the older you get, the more likely you are to forget to take your medication [18]. Nevertheless, our results were similar to those found by Laher et al [22]. The reasons for this statistically significant association ($P<0.05$) in our study,

would be justified by the fact that, at the age of 50, men become increasingly conscious of their lives and responsibilities. They therefore tend to think more about their children's future, so that their health becomes a priority.

Duration of treatment did not show statistically significant results in our study, in contrast to results found in other studies [2, 3, 20, 21]. It is likely that these patients who are on long term treatment, might assume that they have been cured of the disease, prematurely. Therefore, they could deem it unnecessary to continue taking their medication.

The limitations of this study lie entirely on the fact that it was the patients themselves who reported the number of tablets missed in the last month. Other methods of measuring adherence to ART were not used. The identified factors associated with adherence were based entirely on the interview process. Participants came mainly from different communities in the city of Lubumbashi, so our results may not reflect the realities of adherence in other urban and rural settings.

5. CONCLUSION

The present study has enabled us to identify some of the predictive factors associated with good adherence among PLHIV in a resource-limited setting. Although there is still a huge challenge to be met in a developing country like the Democratic Republic of Congo with regard to good adherence to ARV therapy among patients with HIV infection. The adherence rate observed in our study should be maintained as this will further enable us to maximize the benefits of antiretroviral treatment on the health status of PLHIV.

ACKNOWLEDGEMENTS

We would like to thank our friends Madame Bibiche Kalindula, Madame Denise, Mme Francine KARAJ, Dr Yav Evariste, Dr Billy Yav and Papa Jelly for their efforts on behalf of this study.

We would like to thank all the patients for their cooperation, patience and willingness to participate in the study. We would also like to gratefully acknowledge the support of the institution for the realization of this study.

COMPETING INTERESTS

No conflicts of interest have been declared among the authors.

AUTHORS' CONTRIBUTIONS

GYN and CS designed the study, performed the statistical analysis, drafted the protocol and the first version of the manuscript. GYN managed the study analyses and the literature search.All authors have read and approved the final manuscript."

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