



Non-Adherence to Antiretroviral Therapy and Factors Affecting Low Medication Adherence Among Incident HIV-Infected at Lerato Clinic in Germiston

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Abstract: *Introduction:* Highly active antiretroviral therapy (HAART) in the management of HIV/AIDS has made it possible to significantly reduce its incidence and its morbidity and mortality. The objective of this study was to identify factors affecting levels of non-adherence to HAART. *Methods:* The investigator conducted a cross-sectional study at Lerato Clinic in Bertha Qxowa Hospital in Germiston, Gauteng, South Africa from September 2019 to December 2019. Were included to participate, those being more than 18 years old, on HAART for at least three months, consenting to participate, and attending the clinic in that period. Non-adherence was defined as taking their medication $\leq 95\%$ of the time. A threshold of non-adherence $>5\%$ was considered high, with $P < 0.05$ statistically significant. *Results:* Of a total of 278 participants in the study, the average age was 41 ± 13 years with a minimum of 19 years and a maximum of 75 years, a male predominance of 56% ($n = 156$); 19% of patients showed adherence $\leq 95\%$, of which 13.31 ($n=37$) were men and 5.4% ($n=15$). High blood pressure, hyperuricemia, hyperglycemia, and LDL-hypercholesterolemia emerged as clinico-biological determinants and associated factors of non-adherence to HAART. People who often found HAART toxic/bad and who often cared for their partners/spouses/parents were at risk of non-adherence. Similarly, people who were busy doing other things and those who "often" cared for a parent were more likely to adhere to HAART. Systolic blood pressure (SBP), uric acid, blood sugar, and LDL cholesterol which showed higher values. *Conclusion:* Effective management of HIV/AIDS requires $<5\%$ non-adherence. At the end of the present study, the factors associated with non-adherence were individuals and cardiometabolic. All these observations affirmed the holistic and multidisciplinary nature of HIV/AIDS care.

Keywords: HIV, HAART, Non-Adherence, Associated Factors

1. Introduction

The advent of HAART in the management of HIV/AIDS has made it possible to significantly reduce its incidence and its morbidity and mortality [1].

Over time, with side effects of HAART and so many other factors, problems with its adherence have come to the fore. Non-adherence to treatment <5% is decisive, and allows optimal control of viral replication and CD4 lymphocytes but also the prevention of complications [2–4].

Knowing that HIV infection affects the life of people living with HIV (PLWHIV) on the psycho-social, somatic, family, cultural, and spiritual levels. It is therefore crucial that the treatment be global and medico-psycho-social. Apart from the intervention of healthcare personnel, the involvement of families and PLWHIV is an essential element for psychosocial care.

It is in this context that the present study aimed to identify the factors associated with non-adherence to HAART.

2. Materials and Methods

2.1. Study-Design

It was a cross-sectional study conducted from September 2019 to December 2019.

2.2. Study Setting

Lerato Clinic is an HIV clinic in Bertha Qxowa Hospital located in Germiston, Johannesburg, South Africa, and was selected as our study setting.

2.3. Study Population

All adult HIV-infected patients were on HAART for at least three months and attended during the same period and the setting management of this study.

2.3.1. Sampling

The sample size calculation used the Raosoft software:

About 150 patients are seen daily Monday to Friday. Of the patients seen daily approximately, 50 are on HAART. Over the study period, it is estimated that we need approximately 278 participants. This assumes a margin of error of 5%, a confidence level of 95%, and a response distribution of 50%. Participants were investigated for factors that are associated with their drug non-adherence based on observing the timing of doses and keeping clinic appointments for drug refills during the period of the study. These patients meeting the criteria for inclusion in the study were invited to participate in the study, examining potential barriers to adherence. The investigator did approach every patient during each daily interview period.

2.3.2. Criteria of Inclusion

Those being more than 18 years old, on HAART for at least three months, consenting to participate, and attending the clinic were included.

2.3.3. Criteria of Exclusion

Patients less than 18 years old, not speaking English, Tswana, or Zulu, those who are not literate, who cannot communicate in the above-selected languages, and patients on HAART with less than three months of treatment were excluded.

2.4. Data Collection

A precoded and standardized questionnaire was used for data collection. It contains five items that briefly ask for demographic (Gender: male/female, Age: ≥ 45 years/ < 45 years, Ethnic group: Black/White/Coloured/Indian, Marital status: Single/Married/Living with life-partner/Widowed/Separated/Divorced, Level of education: Primary/High school/College/University, and status of employment: Full-time/Sessional/None) information and then put six closed-ended and a single open-ended question about potential barriers to HAART adherence that patient might identify.

That questionnaire was adapted from the one which has been used in the Botswana study [1]. Data were not collected on Tuesdays as the day is consecrated for academic meetings. All surveys were confidential and anonymous. They were conducted in private by the principal investigator in a separate room in the clinic, where participants were filling in the questionnaire for 45 minutes. Data were collected from the consenting respondents using self-administered questionnaires with the help of an assistant for language barriers, especially for those who cannot communicate in selected languages. The key variables to examine were demographics.

The investigator used a validated questionnaire modeled after the Adult AIDS Clinical Trial Group adherence instrument that was carried out to identify missed doses over a 1-year interval. The investigator did first a pill count for all eligible patients every working day. After answering the questionnaire, the investigator collected it for analysis. The information was drawn from files and the questionnaire. The result was transferred into a data sheet.

The files were retrieved from the records department with the help of a clerk working in that department. The information retrieved was recorded on to excel spreadsheet. To minimize recall bias, the investigator did ask patients to indicate their non-adherence over the previous day, previous week, previous month, and previous year successively. Non-adherence was defined as taking their medication $\leq 95\%$ of the time. If one is taking a once-daily treatment, it means missing no more than one dose per month, if it is a twice-

daily treatment it means missing no more than three doses per month and if one is taking three times a day treatment it means missing no more than four doses per month.

The investigator determined the percentage of patients surveyed and met the criteria for non-adherence.

Operational Definitions:

Good HAART adherence: Taking $\geq 95\%$ of prescribed HAART [5]. **Hypertension** was defined by a Blood Pressure (BP) $\geq 140/90$ mmHg following measurements obtained at least 2-3 separate visits (1-4 weeks) unless BP $\geq 180/110$ mmHg in the presence of cardiovascular diseases or whatever the BP, and the notion of antihypertensive treatment [6, 7]. **Treated Arterial Hypertension** is considered uncontrolled if: the blood pressure figures are > 140 mmHg for SBP and 90 mmHg for PAD in non-diabetic hypertensives, > 130 mmHg for SBP and 90 mmHg for PAD in diabetic hypertensive, > 130 mmHg for SBP and 90 mmHg for DBP in hypertensives with renal insufficiency, > 150 mmHg for SBP in hypertensives over 80 years old.

A Body Mass Index (BMI) $\geq 25\text{Kg/m}^2$ and $\geq 30\text{ Kg/m}^2$ define, respectively, overweight and obesity [8]. **Diabetes Mellitus** is defined by a fasting blood sugar level ≥ 126 mg/dl or, whatever the blood sugar level, with the notion of antidiabetic treatment [8]. **Moderate Fasting Hyperglycemia** is defined as a fasting blood glucose level between 110 and 126 mg/dl. **Metabolic Syndrome** is defined by the presence of at least 3 of the following criteria: BP $\geq 130/85$ mm Hg, waist circumference > 102 cm (men) and > 88 cm (women), blood sugar at fasting > 110 mg/dl (5.1 mmol/l), HDL-c < 40 mg/dl (1.0 mmol/l) in men and < 50 mg/dl (1.5 mmol/l) in women, triglycerides > 150 mg/dl (1.7 mmol/l).

An increase in HDL cholesterol $\geq 75\text{mg/dl}$ was considered a cardiovascular risk factor [9, 10]. **Non-HDL Cholesterol** is the differential between total cholesterol and HDLc, it summarizes the sum of the two potentially atherogenic fractions of cholesterol, namely LDL cholesterol and VLDL cholesterol. In patients considered at high cardiovascular risk, the non-HDL cholesterol level is between 130 and 159 mg/dl. In patients considered to be at very high cardiovascular risk, this level is between 160 and 189 mg/dl. **A Suppressed Viral Load** was defined by a plasma HIV-RNA level of ≤ 1000 copies/mL and an **Undetectable Viral Load** was < 50 copies/mL [10]. **Increase in C-Reactive Protein (CRP)** ≥ 3 mg/L [11]. **A Uric Acid level** > 7 mg/dl defines hyperuricemia.

2.5. Data Analysis

The analysis was done as follows: Clinical and biological data were summarized in a table format. Statistical tests were performed to compare the characteristics of adherents and non-adherents. To determine the extent to which each factor contributes to HAART treatment non-adherence, after adjusting for confounding, a multivariate binary logistic regression model was used to identify significant and independent determinants of treatment non-adherence. HAART in patients attending the Lerato Clinic at Bertha Qxowa Hospital. The independent variable identified was

non-adherence to HAART therapy. It made it possible to determine the probability associated with the relationship between each explanatory variable (barrier factors) and the nature. Quantitative variables were converted into qualitative variables that were analyzed using the chi-square test. SPSS version 23.1 software was used for all statistical analyses. Criteria for 2-sided statistical significance were defined by a P-value < 0.05 .

2.6. Ethical Approval and Consent to Participate

The study protocol was approved by the Human Research Ethics Committee of the University of Goma, DR Congo REF# UNIGOM/CEM/14/2022), according to the Declaration of Helsinki III recommendations (Helsinki-Declaration-1964-2015-08-20), and approved by Betha Qxowa Hospital to start the research. The researcher took into consideration the fundamental principles of ethical research.

3. Results

The present study focused on 278 patients and showed an average age of PLWHIV of 41 ± 13 years with a minimum of 19 years and a maximum of 75 years, a male predominance of 56% ($n = 156$); 19% of patients showed non-adherence $> 5\%$, of which 13.31 ($n=37$) were men and 5.4% ($n=15$) were female.

Determinants of non-adherence and associated factors

The logistic regression model retained 3 variables as determinants of non-adherence to HAART: only people who "often" found HAART to be toxic/harmful and who "often" took care of their partner/spouse/parent were at risk of nonadherence, but those who cared "often" for a parent were more adherent to HAART. Similarly, people who were 'busy doing something else' than taking antiretroviral therapy were at risk of nonadherence. Therefore, there are other associated factors that would explain non-adherence (Table 1).

Table 1. Determinants of non-adherence and associated factors.

Variables	B \pm ES	Exp(B)	P-value
Toxic/harmful drug			0.056
Never	-5.3 \pm 2.2	0.005	0.015
Rarely	-26.2 \pm 7303	0.000	0.99
Sometimes	-0.53 \pm 1.4	0.589	0.712
Partner/Spouse/Parent Care			0.003
Never	8.4 \pm 2.2	427.6	< 0.001
Rarely	30.6 \pm 7303	1.7E13	0.997
Sometimes	3.2 \pm 1.4	24.4	0.019
busy with other things			< 0.001
Never	5.3 \pm 1.3	195	< 0.001
Rarely	2.4 \pm 0.88	11	0.006
Sometimes	3.2 \pm 1.4	24.4	0.019
Constant	-3.18 \pm 1.1	0.042	0.004

Clinico-biological determinants of non-adherence by factors

The logistic regression model retained 6 variables as determinants of non-adherence to HAART treatment by

the following clinical and biological parameters: Systolic blood pressure, uric acid, glycemia and LDL cholesterol which presented higher values compared to waist circumference and red blood cells which were below normal limits. (Table 2).

Table 2. Determinants of nonadherence by clinical and biological factors.

Variables	B±ES	Exp(B)	p-value
SBP	-0.308 ± 0.102	0.735	0.003
Waist Circumference	0.360 ± 0.101	1.434	<0.001
Uric acid	-0.891 ± 0.292	0.410	0.002
blood sugar	-0.018 ± 0.007	0.982	0.014
LDL Cholesterol	-0.026 ± 0.009	0.974	0.002
Red blood cells	3.229 ± 1.07	25.251	0.003
Constant	1.193 ± 7.4	3.297	0.872

SBP: Systolic Blood Pressure, LDL: Low density lipoprotein

4. Discussion

Non-adherence to HAART in the present study was 19% with a male predominance and the factors associated with it were found. Several individual factors were associated with HAART non-adherence: perception of HAART as toxic to health, involvement of a partner, or multiple personal occupations.

The present study revealed their negative impact responsible for non-adherence to HAART. This study is similar to that of Essomba et al in Douala who in their cross-sectional study found among the associated factors: multiple occupations [12]. Indeed, the busier the PLWHIV is, he is more exposed to non-adherence to HAART by forgetfulness, unlike those who benefited from the support of their partners/spouse/parent in taking the drugs. Psychosocial support finds its place and impacts adherence to HAART.

About the adverse effects of HAART considered in PLWHIV as manifestations of HAART toxicity was associated with non-adherence to HAART in the present study. This form of poorly tolerated HAART rejection was highlighted in the study conducted in Gabon by Nziengui et al. [13]. In this case, it is therefore crucial that the healthcare staff apply themselves to talk with PLWHIV not only about the dosage of HAART, but also about the possible side effects of HAART.

On the clinical-biological level, the determining factors of non-adherence to HAART were cardiometabolic. Systolic arterial hypertension, hyperglycemia, hyperuricemia, hyper LDL-cholesterolemia are associated with the occurrence of cardiovascular and metabolic events. They are associated with a high risk of cardiovascular morbidity and mortality. These disorders were listed in the study by Agbeko et al on 493 PLWHIV on ARVs; it was hypercholesterolemia, hyper LDL-cholesterolemia, hypo HDL-cholesterolemia were found respectively in 41.4%, 23.5% and 17.4% of patients [14]. Agbeko et al in their study, these cardio-metabolic abnormalities were related to HAART and in the present study to non-adherence to HAART. These disorders would expose PLWHIV to cardio-metabolic diseases.

5. Conclusion

HIV/AIDS is one of the major public health problems. Its effective management requires non-adherence < 5%. At the end of the present study, the factors associated with non-adherence were individual (adverse effects considered to be manifestations of HAART toxicity) and cardiometabolic (systolic hypertension, hyperglycemia, hyperuricemia, hyper LDL-cholesterolemia). All these observations affirm that the care of PLWHIV must be holistic and multidisciplinary.

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