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# Correlation between Health-Related Quality of Life and Various Therapeutic Monitoring Parameters of Ivorian HIV-Infected Patients

**Danho Pascal Abrogoua[1,2*], Boua Alexis Thierry Kamenan[1,3], Aimé Brou[1], Konan N'Guessan[1] and Brou Jérôme Kablan[1]**

[1]*Laboratory of Clinical Pharmacy, Pharmacology and Therapeutics, Faculty of Pharmaceutical and Biological Sciences, University of Cocody-Abidjan, Côte d'Ivoire*
[2]*Department of Clinical Pharmacology, University Teaching Hospital of Cocody-Abidjan, Côte d'Ivoire*
[3]*Department of Pharmacy, University Teaching Hospital of Cocody-Abidjan, Côte d'Ivoire*

**Abstract**

**Background:** Health-related quality of life (HRQOL) is an important issue for HIV-infected patients on antiretroviral therapy (ART). The purpose of our study was to highlight particular items of HRQOL correlated to some monitoring parameters during ART in resource-limited settings (RLS): mean CD4 count, adherence, drug side effects (DSE), cotrimoxazole prophylaxis, self-medication and opportunistic infections.

**Methods:** HRQOL and self-medication were evaluated cross sectionally at eighteenth month of ART with 231 Ivorian HIV-infected patients. Our survey was performed using the MOS-HIV questionnaire for HRQOL. The mean CD4 count during ART was determined with values measured at sixth month (M6), twelfth month (M12), eighteenth month (M18). Routine data from clinical visit at M6, M12, and M18 were used to assess longitudinally the quality of adherence, the occurrence of drug side effects and opportunistic infections during ART. These parameters were evaluated by each patient's physician.

**Results:** Regardless of CD4 counts, scores of HRQOL items attached to them were homogeneous, (patients had an equivalent quality of life). Good adherence was significantly correlated with high general health perception scores, and overall quality of life component scores. Physical functioning and cognitive functioning were significantly influenced by the occurrence of DSE; scores of these items were higher without DSE. Considering the global HRQOL scores, the existence or not of cotrimoxazole prophylaxis did not influence differently the HRQOL scores. Patients who practiced self-medication had global HRQOL scores not significantly different from those who did not practice it. However, we found significant correlations between the practice of self-medication and mental health, energy/fatigue and cognitive functioning. The scores of these items were greater in patients not practicing self-medication.

**Conclusion:** Information about therapeutic risks related to incomplete adherence, DSE and self-medication must be a crucial element integrated in counseling for HIV-infected patients to help optimize their HRQOL in RLS.

**Keywords:** HRQOL; HIV/AIDS; Therapeutic monitoring parameters; Antiretroviral therapy; Resource-limited settings

## Introduction

According to United Nations Programme on HIV/AIDS (UNAIDS) report in 2009, Sub-Saharan Africa still bears an inordinate proportion of the global human immunodeficiency virus (HIV) burden. Although the rate of new HIV infections has decreased, the total number of people living with HIV/AIDS (PLWHAs) continues to rise [1]. The overall goal of antiretroviral therapy (ART) is to reduce mortality and morbidity caused by infection (progression to AIDS), with a prevention or a restoration of immune deficiency [2]. If immunovirological effectiveness of ART is essential, other objectives such as improving and maintaining health related quality of life (HRQOL) should be investigated simultaneously. Indeed the evaluation of HRQOL is complementary to the evaluation of the effectiveness of treatment. In general, the term HRQOL refers to physical, psychological and social benefits of chronic disease on patient's life [3]. HRQOL measures are increasingly being recognized as important when comparing the effectiveness of ART and assessing the impact of HIV/AIDS on peoples' lives. The HRQOL is becoming more integrated as an outcome in clinical trials with patients infected with HIV since the early years of introduction of ART [4-7].

Several disease-specific instruments have been developed to measure quality of life of HIV-infected patients, including the Medical Outcomes Study HIV Health Survey (MOS-HIV) [8,9]. The MOS-HIV is a family of instruments that has grown and has become one of the most widely used to assess QOL of HIV-infected patients [10]. HRQOL is an important issue for HIV-infected patients on antiretroviral therapy (ART). This is particularly true for patients living in resource-limited settings (RLS). The use of ART has dramatically changed the prognosis of PLWHAs in Côte d'Ivoire [11-15]. Thus we can note the importance of this treatment on the health of patients and thus their HRQOL.

We found that studies on quality of life of patients in Côte d'Ivoire are rare. It is important to search factors correlated to HRQOL. We chose to analyze the correlation between HRQOL and some therapeutic monitoring parameters: mean CD4 cell count, occurrence of opportunistic infections (OIs), adherence, occurrence of drug side effects, cotrimoxazole prophylaxis and self-medication. These monitoring parameters are not exhaustive but are of interest because some of them are not often used to analyze HRQOL in RLS. In Côte d'Ivoire the determination of CD4 cells counts is recommended in

***Corresponding authors:** Danho Pascal Abrogoua, Pharmacology and Therapeutics, Faculty of Pharmaceutical and Biological Sciences, University of Cocody-Abidjan, 22 BP 1397 Abidjan 22, Côte d'Ivoire, Tel: (00225) 07949478; E-mail: abrogouadp@yahoo.fr

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practice in monitoring of PLWHAs. The immunological monitoring is the main endpoint of ART response assessment in RLS. The main goal of ART is to prevent progression to AIDS with the onset of AIDS defining events including opportunistic infections. The occurrence of OIs during ART has been also a patient monitoring parameter. We also considered other parameters such as adherence and drug side effects. In the study "Trivacan", the incidence of severe side effects leading to ART discontinuation was 10.8% during the first six months of treatment [12]. The important goal of ART to improve HRQOL of patients can be burdened by the negative influence of the nature, severity or number of drug side effects. The rate of treatment failure increases rapidly when adherence decreases [16]. This failure can be correlated with changes in CD4 cells counts in the definition of immunological failure [17]. It is important to optimize adherence for successful treatment in RLS [18]. The problem of adherence is supported by a series of studies in Africa [19-24], in which the lowest rate was observed in Côte d'Ivoire. It is then advisable to assess the correlation between the level of adherence and the scores of different items of the HRQOL questionnaire in this country. The effect of cotrimoxazole prophylaxis and self-medication of patients on the HRQOL of patients was also evaluated. Eighty percent to 90% of patients on ART also benefit from cotrimoxazole prophylaxis [25]. This chemopropylaxis is recommended for all symptomatic persons (WHO clinical stages 2, 3, or 4) or for any person with a CD4 count <350/mm$^3$, especially in RLS where bacterial infections and malaria are common in PLWHAs. Two randomized clinical trials in Abidjan showed a reduction in morbidity and mortality in PLWHAs on this chemoprophylaxis with varying levels of CD4 cells, with or without tuberculosis [26,27]. Cotrimoxazole prophylaxis therefore influences significantly the health status of patients. But what could be the components of a HRQOL questionnaire most influenced by this prophylaxis? We have investigated these various parameters related to ART monitoring and their relationship to HRQOL. It is important to highlight particular items of HRQOL correlated to these therapeutic monitoring parameters in RLS.

## Methods

### Patients

This study was conducted in a certified structure in the care and the monitoring of PLWHAs in Abidjan: Unité des Soins Ambulatoires et Conseils (USAC) of the University Teaching Hospital of Treichville. This clinical study was focused on HIV-infected patients aged at least 15 years, of either gender. We considered therapy-naive patients prior to initiation of ART in this center. Patients were at the eighteenth month of ART and should not be pregnant. Pregnant patients are referred to other centers for therapeutic and medical monitoring. Patient medical follow-up must be regular since the initiation of ART. We recruited 252 patients according to our inclusion criteria. Twenty-one patients were excluded during the study (Figure 1) for different reasons (refusal to answer the questionnaire, missed medical appointment at M18, pregnancy, and death).

### Medical data and investigation method

This study is a cross-sectional survey on HRQOL of 231 PLWHAs at eighteenth month of ART. Self-medication was also evaluated cross-sectionally at eighteenth month of ART with a questionnaire. The questionnaire regarding self-medication and HRQOL was subject to the patient after their understanding and consent. It was a self-report questionnaire with the presence of an investigator in the medical center. For the patient unable to complete this form itself (low literacy level), the interview of the patient and the filling of the sheet are performed by the investigator. Other monitoring data (mean CD4 cell count, occurrence of opportunistic infections (OIs), adherence, occurrence of drug side effects and cotrimoxazole prophylaxis) were collected retrospectively from patient medical file managed by each patient's regular physician. Data were from the routine monitoring of patients with the prior approval of the administrative health authority.

Our survey on the HRQOL of PLWHAs was performed using the MOS-HIV questionnaire. The MOS-HIV Health Survey consists of 35 questions which assess 10 dimensions of health-related quality of life including general health perceptions, physical functioning, role

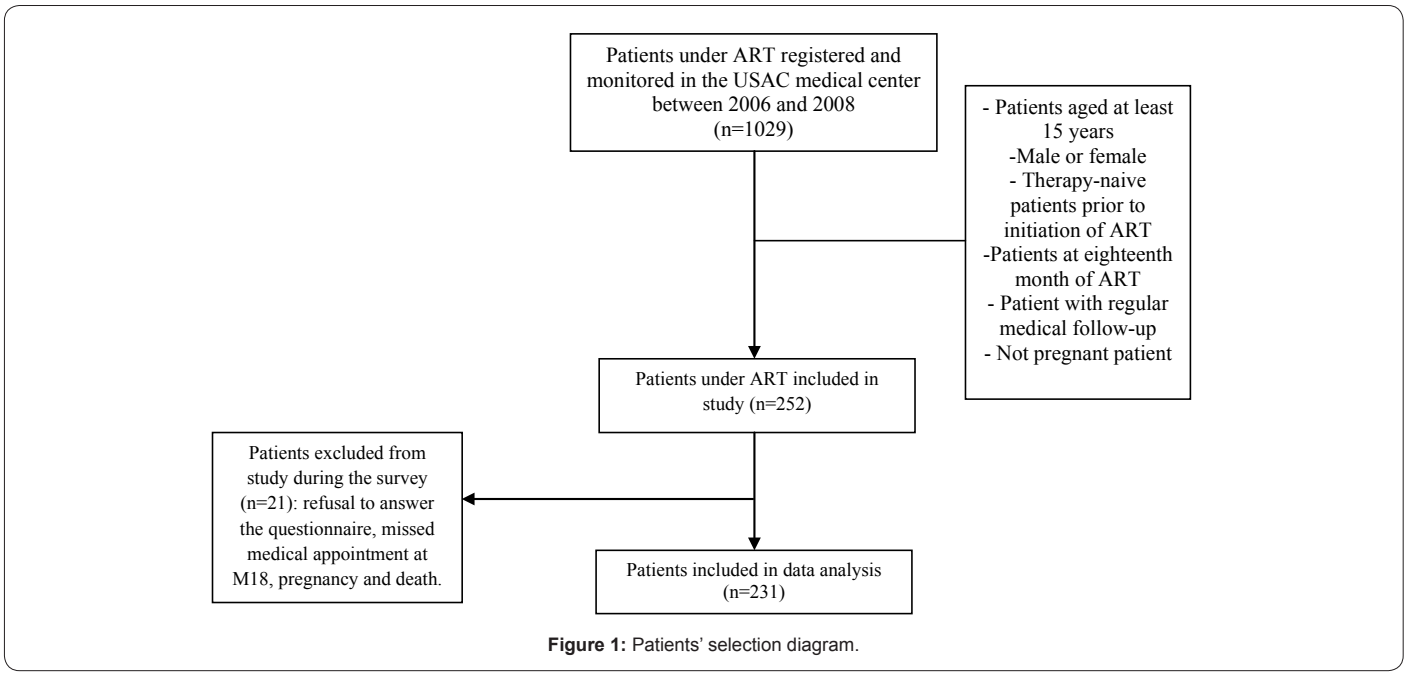


**Figure 1:** Patients' selection diagram.

functioning, pain, social functioning, mental health, energy, health distress, cognitive functioning, quality of life. In addition, one item assesses health transition. All items and scales in the MOS-HIV Health Survey are scored so that a higher score indicates better health status. The evaluation of the quality of life through the various items begins with the listing of responses between a minimum score and maximum score. Patients' responses are listed in order of increasing well-being. The next step in evaluating the quality of life of PLWHAs by MOS-HIV is to convert the scores for each concept. The subscales of the MOS-HIV are scored as summated rating scales on a 0 - 100 scale [28]. The overall HRQOL score for each patient is the average of scores (0-100) of all items of the questionnaire. For example by scoring Social Functioning, patients must answer to one question. The Six responses proposed are coded 1 (minimum score) to 6 (maximum score) in order of increasing social well-being. Then, using the transformation formula for the Social Functioning scale [Lsocial = (100/(6-1)) * (Social Function raw score-1)], 100 is equal to the highest possible score in the transformation; 6 = the top of the range for the sum of the untransformed item scores, while 1 is equal to the lowest possible score of the untransformed scale. A raw score of 4 on the Cognitive Functioning scale would be transformed as follows: Lsocial = (100/(6-1)) x (4-1) = (20 x 3) = 60.

We considered the median value of mean CD4 count during ART with the values measured at M6 (sixth month), M12 (twelfth month), M18 (eighteenth month) for each patient. The CD4 cells counts were determined by the technique of flow cytometry (FACSCalibur, Becton Dickinson, NY-USA).

The occurrence of OIs, drug side effects and the quality of adherence were assessed by each patient's regular physician during his routine medical follow-up. We considered data from clinical visit at M6, M12, and M18 to assess longitudinally the quality of adherence, the occurrence of drug side effects and OIs from the initiation to the eighteenth month of ART. Adherence must be noted as good by the regular physician at each clinical visit before considering a patient as adherent when HRQOL was assessed at the eighteenth month.

| | | | |
|---|---|---|---|
| Age | median (IQR) | | 38 (33-46) |
| | >50 years, n(%) | | 30 (13) |
| | ≤50 years, n(%) | | 201 (87) |
| Female | | | 160 (69.26) |
| HIV type 1, n(%) | | | 221 (95.67) |
| Baseline CD4 cells count | median (IQR) | | 148 (78-220) |
| | <200/mm3, n(%) | | 158 (68.4) |
| | ≥200/mm3, n(%) | | 73 (31.6) |
| Karnofsky score, median (IQR) | | | 90 (90-90) |
| CDC Clinic stage | stage A or B, n(%) | | 172 (74.46) |
| | stage C, n(%) | | 59 (25.54) |
| Presence of opportunistic infections, n(%) | | | 158 (68.4) |
| | NNRTI-based regimens | NVP-based regimen, n(%) | 192 (88.9) |
| | | EFV-based regimen, n(%) | 24 (11.1) |
| | PI-based regimen, n(%) | | 9 (3.9) |
| | 3 NRTIs regimen, n(%) | | 6 (2.6) |
| Cotrimoxazole prophylaxis, n(%) | | | 208 (90) |
| Socio-economic condition | Low condition, n(%) | | 185 (80.10%) |
| | Medium or high condition, n(%) | | 46 (19.9%) |
| Housing condition | Standing, n(%) | | 110 (47.7%) |
| | Modest, n(%) | | 115 (49.8%) |
| | Precarious, n(%) | | 6 (2.6%) |
| Education | Illiteracy or primary school level, n(%) | | 137 (85.7%) |
| | Secondary or high school level, n(%) | | 94 (40.7%) |

IQR: interquartile range

**Table 1:** Patients' baseline features.

Adherence was assessed with low-cost methods in RLS: interview and respect of medical appointments. Respect of medical appointments means also respect of appointments to the pharmacy for replenishment of antiretroviral drugs (ARVs). A general analysis on the review of access to ART in Côte d'Ivoire, confirmed that the methods of assessing adherence most commonly used are the respect of appointments and interviewing patients during consultations or prescription refills at the pharmacy [29]. The occurrence of drug side effects was assessed during the clinic visit by each patient's regular physician. During the assessment of the self-medication through a questionnaire by self-report, patients had to confirm the practice of self-medication answering "yes" or "no". Those who confirmed it have indicated the type of treatment used by self-medication in combination with ARVs among traditional medicine, vitamins, dietary supplements or other treatments to be specified (illicit or not).

### Statistical analysis

Data analysis was conducted using the SPSS software version 14.0 (SPSS Inc., Chicago, Illinois, USA). Median values of HRQOL scores were determined and Mann-Whitney test was applied because it was more appropriate than ANOVA. A P-value of 0.05 was used for all statistical tests.

## Results

### General baseline characteristics

A total of 231 patients was selected with a median age of 38 years (interquartile range, IQR: 33-46) and 69.26% was female. Patients eligible for ART were mainly symptomatic (CDC clinical stage B) with CD4 cells counts <350/mm$^3$. The median value of baseline CD4 cells count was 148/mm$^3$ (IQR: 78-220). The antiretroviral regimen was predominantly made up of the association of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and one Non-Nucleoside Reverse Transcriptase Inhibitor [NNRTI] (93.5%). The NNRTI was either nevirapine [NVP] (88.9%) or efavirenz [EFV] (11.1%). Only 4.76% of patients discontinued treatment just for a substitution of ARVs. All baseline features are presented in table 1. These baseline features were defined as the pre-HAART patient' characteristics.

### Scores of quality of life and therapeutic monitoring parameters

**Scores of quality of life and adherence:** We noted that 88.74% of patients were adherent during the medical follow-up period considered in our study. According to the global HRQOL scores recorded, the adherent patients had a significantly better quality of life compared to non-adherent patients (p = 0.01) (Table 2). We also observed significant correlations between some HRQOL items and adherence. Significant relationships were found between general health perception (p = 0.04), overall quality of life component (0.04) and adherence: scores of these items were greater in adherent patients (Table 2). This also means that good adherence was significantly correlated with high general health perception and overall quality of life component scores. Other items in the questionnaire had HRQOL scores not significantly different according to whether patients were adherent or not. The scores of these items in the HRQOL questionnaire were statistically homogeneous in all patients even if some scores were higher among adherent patients.

**Scores of quality of life and drug side effects:** Drug side effects were reported in 20.8% of patients during the clinic follow-up. Among drug side effects identified, peripheral neuropathy (58.24%), anemia (13.18%) and digestive disorders (09.9%) were most important. Headache, sleep disorders and skin reactions (pruritus, rash), Steven Johnson syndrome, hypotension and mucocutaneous hyperpigmentation were also identified (Figure 2). Thirty-one (64.58%) patients reporting drug side effects have practiced self-medication. According to the global HRQOL scores recorded, patients who had no drug side effects had a better HRQOL (Table 2) compared to those who experienced drug side effects ($p = 0.03$). We also found statistically significant correlations between the occurrence of drug side effects and physical functioning ($p = 0.02$) and cognitive functioning ($p = 0.04$) (Table 2); the scores of these items were higher without drug side effects. Other items in the questionnaire had HRQOL scores not significantly different according to the occurrence of drug side effects or not: the scores of these items related to patients who experienced drug side effects and those who did not have, were statistically homogeneous.

**Scores of quality of life and self-medication:** Fifty-eight percent of patients on ART practiced self-medication in our study. In the practice of self-medication, over three-quarters of patients (76.12%) noted the use of products from traditional medicine. About a quarter of patients (25.4%) discussed the use of street drugs without specifying their therapeutic class. Patients using dietary supplements and vitamins were also quite significant with respective proportions of 22.4% and 15%. One noted the use of antibiotics but we could not determine whether they were from a pharmacy or street drugs. Two patients used

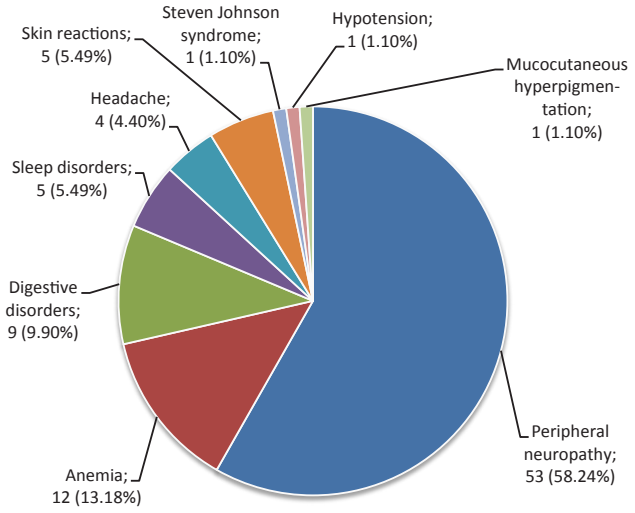


**Figure 2:** Drug side effects during the monitoring period.

| HRQOL Questionnaire items | HRQOL items scores [median (IQR)] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Adherence | | | Drug side effects | | | Self-medication | | |
| | Yes (n=205) | No (n=26) | p | No (n=183) | Yes (n=48) | p | No (n=97) | Yes (n=134) | p |
| **Global HRQOL score** | 80.98 (73.76-87.22) | 75.44 (70.11-81.89) | 0.01 | 81.27 (73.76-87.36) | 78.23 (72.04-82.62) | 0.03 | 81.11 (74.42-87.97) | 80.12 (71.64-85.91) | 0.08 |
| **GHP** | 60 (50-70) | 55 (45-65) | 0.04 | 60 (50-70) | 60 (50-70) | 0.69 | 60 (50-70) | 60 (50-70) | 0.88 |
| **PF** | 100 (91.66-100) | 91.66 (66.66-100) | 0.05 | 100 (91.66-100) | 91.66 (83.33-100) | 0.01 | 100 (91.66-100) | 100 (91.66-100) | 0.07 |
| **RF** | 100 (100-100) | 100 (100-100) | 0.68 | 100 (100-100) | 100 (100-100) | 0.55 | 100 (100-100) | 100 (100-100) | 0.31 |
| **P** | 77.77 (55.55-100) | 66.66 (44.44-100) | 0.14 | 88.88 (55.55-100) | 66.66 (55.55-100) | 0.24 | 100 (55.55-100) | 66.66 (55.55-100) | 0.10 |
| **SF** | 100 (100-100) | 100 (100-100) | 0.26 | 100 (100-100) | 100 (100-100) | 0.44 | 100 (100-100) | 100 (100-100) | 0.34 |
| **MH** | 68 (56-80) | 68 (52-76) | 0.77 | 68 (56-80) | 64 (52-78) | 0.20 | 72 (56-80) | 68 (56-76) | 0.04 |
| **EF** | 85 (70-90) | 80 (65-90) | 0.32 | 85 (70-95) | 77.50 (62.5-90) | 0.05 | 85 (70-95) | 80 (70-90) | 0.03 |
| **HD** | 95 (80-100) | 92.5 (65-100) | 0.38 | 95 (80-100) | 92.5 (72.5-100) | 0.49 | 100 (80-100) | 95 (75-100) | 0.13 |
| **CF** | 90 (80-100) | 85 (75-100) | 0.22 | 95 (80-100) | 87.5 (70-100) | 0.03 | 95 (85-100) | 85 (75-100) | 0.007 |
| **QL** | 75 (50-100) | 50 (50-75) | 0.04 | 75 (50-100) | 75 (50-100) | 0.34 | 75 (50-100) | 75 (50-100) | 0.43 |
| **HT** | 75 (50-75) | 50 (50-75) | 0.15 | 75 (50-75) | 75 (50-75) | 0.96 | 75 (50-75) | 75 (50-75) | 0.76 |

p: Mann-Whitney test, IQR: interquartile range; GHP: General Health Perceptions, PF: Physical Functioning, RF: Role Functioning, P: Pain, SF: Social Functioning, MH: Mental Health, EF: Energy/Fatigue, HD: Health Distress, CF: Cognitive Functioning, QL: Quality of Life, HT: Health Transition.

**Table 2:** HRQOL scores related to adherence, drug side effects and self-medication.

some products without specifying their nature. We noted that some patients have combined different products cited in self-medication. According to the global HRQOL scores determined (table 3), patients who practiced self-medication had a quality of life not significantly different from those who did not practice (p = 0.08). But we have found significant correlations between the practice of self-medication and mental health (p = 0.046), energy/fatigue (p = 0.03) and cognitive functioning (p = 0.007) (Table 3): the scores of these items were greater in patients not practicing self-medication. This means that the practice of self-medication was significantly correlated with low energy/fatigue scores, low mental health scores and low cognitive functioning scores. Other HRQOL items had scores not significantly different according to the practice of self-medication or not. The scores of these items related to patients practicing self-medication and those of patients who did not practice it, were statistically homogenous even if some scores were higher in the latter group. According to our findings, adherence had a positive effect on different items of HRQOL and self medication had a negative effect. But there was not a correlation between adherence and self medication (chi-square test, p=0.972).

**Scores of quality of life and immunological and clinical parameters:** We noted increasing gains of CD4 counts with values of +113, +153.8 and +179.2 respectively at M6, M12 and M18 compared to baseline CD4 count. We found no significant relationships (Table 3) between the mean of CD4 cell counts during ART and scores of different HRQOL items including global HRQOL scores. Whatever the values we considered for the mean CD4 cell count, HRQOL scores attached to them were statistically homogeneous. Twenty-nine OIs were identified during the follow-up period. Tuberculosis (41.38%) was the most important OI identified. We noted also in decreasing frequencies other OIs: oropharyngeal candidiasis, extrapulmonary cryptococcosis, shingles, herpes simplex infection, Kaposi's sarcoma and chronic diarrhea (Figure 3). The occurrence of OIs during ART did not significantly affect the different HRQOL items scores including global HRQOL scores (Table 3).

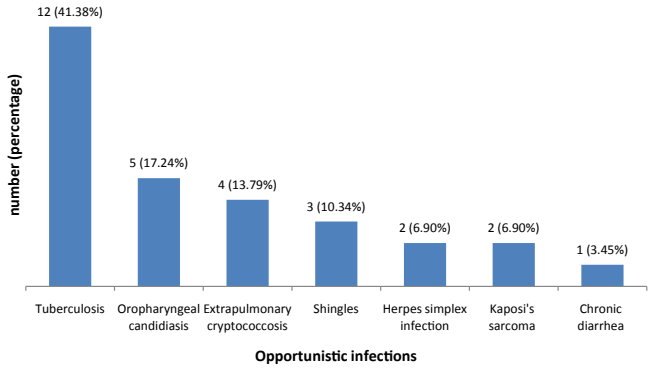


**Figure 3:** Opportunistic infections during the monitoring period.

| HRQOL Questionnaire items | HRQOL items scores[median (IQR)] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean CD4 count (/mm3) | | | OIs during ART | | | Cotrimoxazole prophylaxis | | |
| | ≤ 350 (n=150) | > 350 (n=81) | p | No (n=73) | Yes (n=158) | p | No (n=23) | Yes (n=208) | p |
| Global HRQOL score | 80.83 (72.85-86.91) | 80.06 (73.98-86.76) | 0.97 | 80.52 (72.74-86.84) | 81.21 (75.6-87.36) | 0.45 | 77.79 (73.05-83.36) | 80.96 (72.95-87.23) | 0.22 |
| GHP | 60 (50-70) | 60 (50-70) | 0.68 | 60 (50-70) | 65 (55-70) | 0.43 | 60 (50-70) | 55 (45-65) | 0.23 |
| PF | 100 (91.66-100) | 100 (91.66-100) | 0.80 | 100 (91.66-100) | 100 (100-100) | 0.06 | 100 (91.66-100) | 100 (91.66-100) | 0.67 |
| RF | 100 (100-100) | 100 (100-100) | 0.54 | 100 (100-100) | 100 (100-100) | 0.24 | 100 (100-100) | 100 (100-100) | 0.73 |
| P | 77.77 (55.55-100) | 77.77 (55.55-100) | 0.45 | 77.77 (55.55-100) | 77.77 (55.55-100) | 0.85 | 77.77 (55.55-100) | 66.66 (55.55-100) | 0.97 |
| SF | 100 (100-100) | 100 (100-100) | 0.07 | 100 (100-100) | 100 (100-100) | 0.82 | 100 (100-100) | 100 (100-100) | 0.71 |
| MH | 68 (60-80) | 68 (56-80) | 0.49 | 68 (56-80) | 72 (60-80) | 0.21 | 68 (56-80) | 68 (52-76) | 0.47 |
| EF | 85 (70-90) | 80 (65-95 | 0.93 | 82.50 (70-90) | 90 (75-100) | 0.13 | 75 (55-90) | 85 (70-90) | 0.09 |
| HD | 95 (80-100) | 95 (75-100) | 0.64 | 95 (77.5-100) | 95 (80-100) | 0.97 | 95 (80-100) | 100 (75-100) | 0.54 |
| CF | 90 (80-100) | 90 (75-100) | 0.99 | 90 (77.5-100) | 95 (80-100) | 0.51 | 90 (75-100) | 85 (80-100) | 0.78 |
| QL | 75 (50-100) | 75 (50-75) | 0.98 | 75 (50-100) | 75 (50-75) | 0.17 | 75 (50-100) | 75 (50-75) | 0.47 |
| HT | 75 (50-75) | 75 (50-75) | 0.95 | 75 (50-75) | 75 (50-75) | 0.27 | 75 (50-75) | 50 (50-75) | 0.82 |

p: Mann-Whitney test, IQR: interquartile range; OIs: opportunistic infections; GHP: General Health Perceptions, PF: Physical Functioning, RF: Role Functioning, P: Pain, SF: Social Functioning, MH: Mental Health, EF: Energy/Fatigue, HD: Health Distress, CF: Cognitive Functioning, QL: Quality of Life, HT: Health Transition.

**Table 3:** HRQOL scores related to mean CD4 count, cotrimoxazole prophylaxis and OIs during ART.

**Scores of quality of life and cotrimoxazole prophylaxis:** Considering the global HRQOL scores (table 3), the existence or not of cotrimoxazole prophylaxis did not influence differently the HRQOL scores ($p = 0.23$). There was also no significant differences between scores of HRQOL items and the fact that patients were on cotrimoxazole prophylaxis or not (Table 3). Ninety percent of patients were on cotrimoxazole prophylaxis in our study. HRQOL scores that are attached to patients on this chemoprophylaxis and those not eligible for it were statistically homogeneous.

## Discussion

In our study whatever the mean CD4 cell count, patients had an equivalent quality of life according to median scores of individual items of HRQOL questionnaire. According to Gill et al., efforts to improve CD4 cells counts of patients are also likely to improve the quality of life [30]. In their study, high CD4 cells counts were associated with better quality of life [30]. By improving CD4 cell levels regardless of the baseline value, ART appears to improve the quality of life for all patients. Our patients started ART with a median baseline CD4 cell count equal to 148/mm$^3$ (IQR: 78-220). Therefore, patients with mean CD4 count ≤ 350/mm$^3$ during treatment did not necessarily have unfavorable immunological changes.

In our study, the occurrence of OIs during ART did not significantly affect the HRQOL scores. The effective management of OIs has long been integrated into the therapeutic monitoring of PLWHAs in RLS. It ensures a better chance of improving as quickly as possible the overall health of patients with OIs in association with the use of ARVs.

However, other studies have shown that the quality of life of patients on ART may vary depending on the clinical condition. In a trial of ART for symptomatic and asymptomatic HIV-infected patients, only the previously symptomatic patients experienced an improvement in their HRQOL, while initially asymptomatic patients reported an actual decline. Although this improvement was limited to cognitive and social functioning, they can be considered as highly relevant aspects of patients QOL [31].

According to the global HRQOL scores, the adherent patients had a better HRQOL compared to others. But not all the items of HRQOL were correlated to adherence. Only general perception of health and overall quality of life were significantly affected by the quality of adherence. Quality of life seems an important variable of patients' adherence. Indeed, Mannheimer et al. had already pointed out, in a longitudinal study of 996 PLWHAs, that patients who kept adherence over a period of 12 months showed a high level of HRQOL [32]. Delmas et al. [33] arrived at similar results. The comparative results of this study between groups of adherent and non-adherent patients attempt to strengthen the observation that adherent patients had a higher level of quality of life than non-adherent ones. The results of this longitudinal study have shown that physical health was associated with adherence. The adherent patients showed high HRQOL scores at the physical functioning. Cunningham et al. showed that physical health is a predictor of survival in patients with HIV/AIDS [34]. These results appear consistent, because if patients who have a high level of physical health are those who adhere to HAART, it is likely that the evolution of HIV/AIDS has stabilized, as well as its adverse consequences. The physical dimension includes physical function, daily activities, pain and energy/fatigue. If the physical dimension is an important reflection of general health and quality of life of the adherent patients, as it has been shown in the studies of Delmas [33] and Cunningham [34], we find logical that the components "general health perception" and "overall quality of life" were also influenced by adherence in our study. Efforts should always be made to improve adherence in order to also improve HRQOL.

According to the global HRQOL scores, patients with no drug side effects had significant improved quality of life compared to others. But all the HRQOL items were not correlated to the occurrence of drug side effects. Only physical functioning and cognitive functioning were significantly influenced by the occurrence of drug side effects. It is necessary to note that drug side effects reported in this study were physical events. The observation that ART negatively impacts physical functioning has other precedents. Early studies of azidothymidine (AZT) monotherapy noted that improvements in HRQOL were offset by the severity of AZT-induced side effects [35,36]. Gill et al. have shown that ART had an independent negative effect on physical functioning [30]. According to these authors, these results suggest in their interpretation, that ART affects physical functioning in two ways. First, it has a direct effect on physical functioning, reflecting the inherent toxicity of ARVs that is negative. Second, it has an indirect effect due to viral suppression and increased CD4 cells counts, that is positive. For any individual, the net effects depend on the balance of these effects. For patients who start out with at least some deficits in physical functioning, the net effect of ART on physical function should be positive because the indirect positive effects with elevated CD4 cells counts and undetectable viral load outweigh the negative direct toxic effects of ART [30]. Not only the complexity of ARV regimens affects the quality of life of a patient, but it has become a major obstacle for adherence, which is one of the main determinants for successful ART, as that has been shown in many studies [37-42]. In the study of Fumaz et al., HRQOL increased in group patients treated with efavirenz-based regimens during the follow-up compared to the HRQOL at baseline. When patients were asked about the reasons for this increase, nearly three-quarters felt that this treatment had the lowest impact on their daily life because of its greater simplicity and that it had improved their HRQOL [43].

Overall in our study, the existence of cotrimoxazole prophylaxis, as well as the practice of self-medication did not differently influence the patients' HRQOL. The cotrimoxazole prophylaxis in reducing morbidity and mortality among PLWHAs in RLS tends to make consistent scores of HRQOL for those not yet eligible for this prophylaxis.

Specific links were found between the practice of self-medication and some items of the HRQOL questionnaire such as mental health, energy/fatigue and cognitive functioning. In their study of adherence in clinical practice in Abidjan [23], Eholie et al. have shown that most of the reasons given by patients for not taking ARVs were similar to those reported by other African researchers: lack of money, repeated stock-outs of ARVs, fear of drug side effects and negative influence of traditional healers [44,45]. As for the latter reason, in their experience, these patients discontinued ART at the request of traditional healers. This suggests that efforts are needed to improve the integration of traditional healers in care related to HIV infection in order to maximize adherence to ART. This is more crucial in rural areas, where traditional healers are more numerous and more accessible than modern physicians. The self-medication may be due to the search for additional benefits on patients' health but these benefits could be placebo effects. The many side effects of ARVs may push patients to self-medication when it could be, itself, a source of side effects and toxic events. ARVs cause many interactions among themselves and with other drugs used in the treatment of PLWHAs. These interactions, most commonly known, monitored with possible dose adjustments guide an optimal medical

prescription. The use of various products from self-medication with unknown pharmacological mechanisms is a source of potential drug-drug interactions between themselves and between them and ARVs. These uncontrolled drug-drug interactions can influence dramatically ART response. One or more questions on each of the four main determinants of mental health (anxiety, depression, loss of control of emotional behavior and psychological well-being) are included in this concept [46]. Our patients practicing self-medication with lower scores of "mental health" and "cognitive function", are more prone to seek complementary alternatives therapeutic associated to ARVs, probably in search of a moral satisfaction or a complementary therapeutic security. Wang et al. [47] who showed in their study that over 70% of patients using narcotics had physical disabilities and mental disorders compared to patients using only ARVs. In the notion of "market street drugs" and products not specified in self-medication, narcotics are not excluded with our patients.

## Limitations

Our study has several limitations that need to be highlighted. A limitation of this study was that we did not search during our survey if patients answering "yes" to self-medication were practicing it continually or punctually. Another limitation is related to the assessment of adherence with low incomes methods which did not permit us to quantify adherence level of each patient. It would be more interesting to correlate adherence rates to HRQOL scores in RLS. Quantifying the levels of medication adherence involved PLWHAs care has been the focus of many studies. It will not be easy to compare our results on the correlation of HRQOL and adherence to other findings related to quantified adherence levels in a similar study. However, it should be noted that it is not often easy to find quantified values of adherence levels in routine monitoring of patients in RLS.

## Conclusion

Regardless of the values we considered for the mean of CD4 cells counts during ART, the scores of HRQOL items attached to them were homogeneous. Whatever the mean CD4 cell count, patients had an equivalent quality of life. Good adherence was significantly correlated with high general health perception scores and overall quality of life scores. Efforts should always be made to improve adherence in order to also improve HRQOL in RLS. The management of drug side effects must be optimal in order to minimize their influence on HRQOL because these drug side effects influence directly the patients' HRQOL and may affect adherence to ART. Physical functioning was particularly influenced by drug side effects that were mostly made up of physical events in our study. Cotrimoxazole prophylaxis in reducing morbidity and mortality in PLWHAs tends to make their quality of life equivalent to that of patients who do not use this chemoprophylaxis. Self-medication should not be recommended to our patients: products from self-medication may constitute a major risk of occurrence of toxic events, negative drug-drug interactions and ineffective treatment. Information about therapeutic risks related to incomplete adherence, drug side effects, self-medication must be a crucial element integrated in counseling session for HIV-infected patients in order to improve their global HRQOL in RLS.

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