Original Article

The Association between Antiretroviral Therapy with Depression and Health Related Quality of Life in Patients Infected with HIV in Kasempa, Zambia

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ABSTRACT

Background: Many HIV-infected patients are accessing antiretroviral therapy (ART) in Zambia. This has enabled them to live longer. However, it is necessary to determine whether such improvements are accompanied with parallel improvements in quality of life. The purpose of this research was to determine whether ART was associated with lower levels of depression and higher levels of health-related quality of life (HRQOL).

Objectives: The primary objective was to compare the association of ART with depression and Health Related Quality of Life (HRQOL) in treatment naïve and treatment experienced patients. The specific objectives were to screen for levels of depression and HRQOL in HIV infected patients, and to compare these levels between ART-experienced and ART-na¿ve patients.

Methods: This was a cross sectional study in which 140 HIV-infected adults (70 ART-experienced and 70 ART-naïve) in Kasempa district were enrolled by convenient sampling. Independent variables of sex, age, marital status, education and employment status were matched across the two groups to avoid their confounding effect and bias. Depression and HRQOL were screened using the Centre for Epidemiologic Studies – Depression (CES-D) and Medical Outcomes Survey – HIV (MOS-HIV) tools respectively in both groups. The average scores for depression in both groups were compared using the t-test. Mental Health Summary scores (MHS) and Physical Health Summary scores (PHS) derived from the MOS-HIV tool were obtained by factor analysis and linearly transformed into a 0-100 scale. These scores were also compared between the two groups using the t-test. Multiple linear regression was used to determine the factors that were significantly associated with depression and HRQOL in both groups.

Results: The mean depression scores were found to be lower among ART-experienced clients compared with their ART-naïve counterparts with a mean difference of 7.40 (95% C.I 3.77-11.03; $P < 0.0001$). Overall, ART-experienced participants had higher HRQOL scores compared with their ART- naïve counterparts with differences of 23.0 (95% C.I 16.0-30.1; $P < 0.0001$) and 11.2 (95% C.I 6.0-16.4; $P < 0.0001$) in MHS and PHS scores respectively.

Conclusion: Being ART-experienced was associated with lower depression scores and higher HRQOL scores when compared with being ART-naïve. Lower depression scores and higher HRQOL scores were associated with being male, married, single, asymptomatic and having higher CD4 counts.

INTRODUCTION

The 2011 Joint United Nations Programme on HIV/AIDS (UNAIDS) report showed that there was a reduction in the number of AIDS-related deaths globally, from 1.9 million in 2001 to 1.8 million deaths in 2010 and that many HIV-

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infected persons are now accessing antiretroviral therapy (ART) which has led to a reduction in the number of HIV related deaths in the recent years. According to the World Health Organisation (WHO) Global Health Observatory Data, the number of HIV-infected persons accessing ART has increased from 690,000 in 2000 to 14.9 million people in 2014 globally. The number of HIV infected persons taking ART in Zambia has increased from 344,407 in 2010 to 671,066 in 2014 while annual HIV-related deaths have reduced from 58,000 in 2010 to 19,000 in 2014 according to the UNAIDS Global AIDS Response Progress Report (GARPR) on Zambia.

The primary objective of ART is to reduce HIV viral replication and thereby reduce the morbidity and mortality of HIV-infected patients. And since its advent in 1996, ART has led to a drastic reduction in HIV-associated mortality.[1,2,3] Therefore, HIV-infected persons are now living longer. However, despite the reduction in mortality and morbidity caused by ART, HIV-infected persons continue to experience depression and poor health related quality of life (HRQOL).[8,9,10]

It has therefore become important to determine the association between ART and levels of depression and HRQOL in these patients. There is need to determine whether the improvements in morbidity and mortality brought about by ART are associated with lower depression and higher HRQOL scores in these persons. The purpose of this study was to determine the association of ART with depression and HRQOL in HIV infected adults at Mukinge Mission Hospital and Kasempa Urban Clinic (KUC) in Kasempa district of Zambia.

METHODS

Study Setting: The research was conducted in a rural setting in Kasempa, one of the districts in North-western province of Zambia. The district in 2014 had a projected population of 79,794 persons according to the Central Statistics Office (CSO). Interviews were conducted at the out-patient ART Clinics at both Mukinge Mission Hospital and Kasempa Urban Clinic (KUC). The facilities are only 7 kilometres apart and are both accredited to offer ART services.

Study Population: HIV-infected adults aged 18 years and above attending ART clinics at Mukinge Mission hospital and KUC were enrolled. Clients receiving ART (ART-experienced) and those that had not yet been started on ART (ART-naive) were both enrolled into the study. All participants needed to have had an HIV diagnosis that was made three months or more prior to this research, and the ART-experienced clients needed to have been on ART for at least three months.

Study Design: This was a Cross sectional study in which levels of depression and health-related quality of life (HRQOL) between ART-experienced participants and ART-na¿ve participants were compared..

Sampling: By convenient sampling, a total of 140 participants were enrolled, into the two equal groups or arms as ART-naive (70 participants) and ART-experienced (70 participants). And in order to facilitate comparison of depression and HRQOL between the two groups of participants, independent variables of age, sex, marital status, education and employment status were controlled by matching. This meant that for each of these variables, equal numbers of participants were for enrolled between the two arms because various studies have shown that these variables have a significant effect on depression and HRQOL.[4,5,6,7] The matching was done in order to minimise the confounding effect of these variables as they can interfere with the association of ART with depression and HRQOL.

Variables

Dependent variables:

a. **Depression scores** derived from the CES-D questionnaire
b. **HRQOL scores:** The two **summary scores** namely, Mental Health Summary score (MHS) and Physical Health Summary score (PHS).

Independent Variables:

a. **Socio-demographic characteristics:** Age, sex, marital status, education background, employment status
b. **Clinical factors:** Latest CD4 count, presence of symptoms/signs (Based on WHO clinical Stages)**,** time since HIV was diagnosed.

Data Collection

Socio-demographic and background: The following information was collected: Age, sex, marital status,

education background, employment status, time since HIV was diagnosed, presence of symptoms (WHO stage) and latest CD4 count.

Depression: The Centre for Epidemiologic Studies Depression (CES-D) scale was used. This tool measures a patient's depressive feelings and behaviour in the previous one week. It is comprised of twenty questions with graded responses from 0 to 3.

Health related quality of life: The Medical Outcomes Survey–HIV (MOS-HIV) questionnaire was used. It contains 35 questions which are grouped into eleven dimensions namely General health perception (GHP), Physical function (PF), Role function (RF), Cognitive function (CF), Body Pain (BP), Mental health (MH), Energy/Vitality (EV), Health distress (HD), Social function (SF), Quality of Life (QL) and Health Transition (HT).

Data Analysis

Data management: The data was analyzed using the Statistical Package for the Social Science version 21 (SPSS-21).

Depression: The mean or average of the depression scores from the CES-D tool for each of the two groups of participants were calculated. Then the student t-test for independent samples was employed to compare these means. The p-value was set at <0.05 and confidence interval (CI) at 95%.

HRQOL: From the MOS-HIV tool, the scores from each of the 11 dimensions for each of the two groups of participants were added and eleven raw mean scores generated. The raw mean scores for each dimension were then subjected to factor analysis with oblique rotation using SPSS. This yielded two summary scores called Physical Health Summary (PHS) score and the Mental Health Summary (MHS) score for the two groups of participants. The MHS and PHS scores between the two groups were then compared using the student t-test for independent samples. The p-value was set at <0.05 and confidence interval (CI) at 95%.

Multivariate analysis: For each of the two groups of participants, multiple linear regression analysis was used to show the variables that significantly influence depression and HRQOL in HIV-infected persons. The independent variables entered in this model were age, sex, marital status, education, employment status, presence of symptoms, latest CD4 count and time since HIV diagnosis was made.

Ethical Considerations

This research had ethical approval by the ERES Converge IRB, Lusaka. Prior to enrolment into this study, informed consent was obtained from participants that were willing using a specific consent form designed for the purpose. The information collected was treated as confidential.

RESULTS

Demographic and clinical characteristics of participants

From Table 1, a total of 140 participants were enrolled. Half 70 (50%) of the participants were ART-naïve and the other half 70 (50%) were ART-experienced. Between the two arms, the number of participants enrolled was matched on the basis of age, sex, marital status, education and employment status. Most of the participants (46%) were in the age categories of 18-34, 35-49 years in both arms respectively.

Table 1: Baseline Socio-demographic Characteristics of Participants

Variable	Variable category	ART-Naïve N = 70(%)	ART-Experienced N = 70(%)
1.Age(Years)	18-34 35-49 -	32(46) 32(46) *6(8)*	32(46) 32(46) *6(8)*
2.Sex	Male Female	35(50) 35(50)	35(50) 35(50)
3.Marital Status	Single Married S/D/W*	9(13) 46(66) 15(21)	9(13) 46(66) 15(21)
4.Education	Pre-secondary Secondary Post-secondary	19(27) 43(61) 8(12)	19(27) 43(61) 8(12)
5.Employment status	Unemployed Employed	27(39) 43(61)	27(39) 43(61)
6. ART Regimen	1st line 2nd line	N/A N/A	66(94) 4(6)
7.Presence of Symptoms	Asymptomatic Symptomatic	42(60) 28(40)	56(80) 14(20)
8. Length on ART	... >1 Year	N/A N/A	10(14) 60(86)
9.Latest CD4 count	≤ cells /µl >350 cells /µl	43(61) 27(39)	18(26)** 52(74)**
10.Time since HIV diagnosis	≤ >1 Year	52(74) 18(26)	13(19)** 57(81)**

*S/D/W : Separated/Divorced/Widowed.
** Statistically significant (P < 0.05) difference between the two groups of participants.

Sixty six percent (66%) of the participants were married in both arms. Participants who were single were in the minority (9%) in both arms. Twenty one percent (21%) of the respondents in both arms were separated, divorced or widowed (S/D/W). Sixty one percent (61%) had attained secondary school education. However, only 12% had attained post-secondary education in both arms. Most of the participants (61%) were in of gainful employment in both arms.

Only 39(%) were not employed. Ninety-four (94%) of ART-experienced participants were on the first-line of ART drugs and only 6% had moved to 2nd line. There were more asymptomatic participants among ART-experienced clients (80%) compared with their ART-naïve counterparts (60%). Most of the participants (61%) among the ART-naïve clients had latest CD4 counts of ≤ 350 cells/ì L whereas among the ART-experienced participants, the majority (74%) had CD4 counts of > 350 cells/ì L. The cut-off of 350 cells/ì L was chosen because this was the threshold for initiating ART at the time of this research. In 74% of ART-naive participants and 81% of ART-experienced participants, the diagnosis of HIV was made more than a year prior to the interview.

Comparison of Depression in ART-naïve and ART-experienced clients

The graph in Figure 1 shows that, ART-naïve participants had higher depression scores with a mean score of 15.97, while their ART-experienced counterparts had lower depression scores with a mean of 8.57. There was thus an average difference in depression scores of 7.40 (SD = 15.4; CI 95%: 3.77–11.03) as shown in Table 2. Using the Student t-test for independent samples, a *P* value of < 0.0001 was derived.

Figure 1

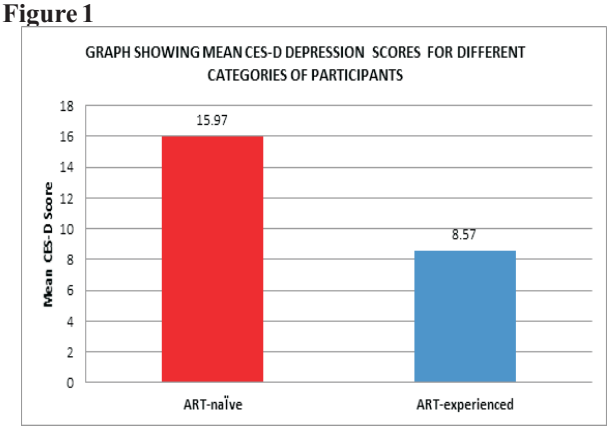

Table 2: MEAN DEPRESSION SCORE DIFFERENCE AND ITS STATISTICAL SIGNIFICANCE

ART-naive	ART-experience	Difference	S.D	95% C.I		*P*
				Lower	Upper	
15.97	8.57	7.40	15.43	3.77	11.03	< 0.0001

The mean difference in depression scores (7.40) between the two arms was statistically significant (p <0.05) using the t-test for independent samples,

Comparison of HRQOL in ART-naïve and ART-experienced clients

Figure 2 shows that on average, ART-experienced participants had higher HRQOL scores in almost all dimensions except for cognitive function (CF) and social function (SF) where the difference was not significant. Table 3 displays the same information and further shows that MHS and PHS components were higher among ART-experienced participants compared with their ART-naive counterparts

Figure 2

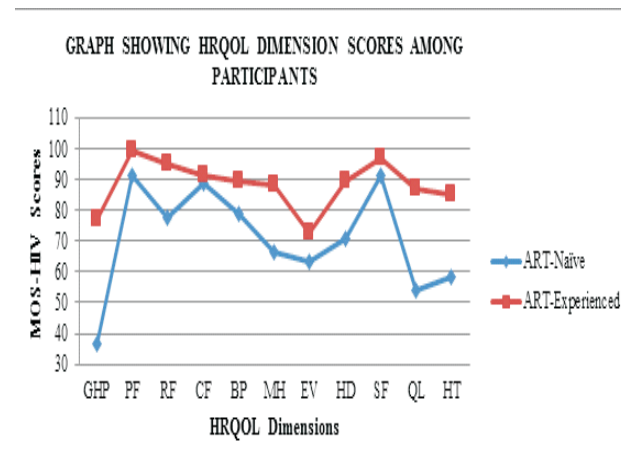

Table 3: MEAN HRQOL DIMENSIONAL SCORES AND SUMMARY SCORE COMPONENTS OF THE ART-NAÏVE AND ART-EXPERIENCED PARTICIPANTS

Dimensions/ Components	Experienced	Naive	Difference	S.D	95% C. I.		*P*
					Lower	Upper	
GHP	76.9	36.8	40.1	43.0	30.0	50.2	.000*
PF	99.4	90.9	8.5	17.6	4.3	12.6	.000*
RF	95.0	77.9	17.1	44.2	6.7	27.6	.000*
CF	91.4	89.1	2.3	23.1	-3.1	7.7	**.203**
BP	89.1	78.6	10.5	32.5	2.9	18.2	.004
MH	88.2	66.6	21.6	36.9	12.9	30.3	.000*
EV	72.7	63.5	9.2	22.9	3.8	14.6	.000*
HD	89.5	71.1	18.4	39.8	9.1	27.8	.000*
SF	96.8	91.4	5.4	29.6	-1.6	12.4	**.063**
QL	86.8	55.4	31.4	43.5	21.2	41.7	.000*
HT	85.3	58.2	27.1	48.9	15.6	38.7	.000*
MHS	**84.1**	**61.1**	23.0	29.8	16.0	30.1	.000*
PHS	**93.3**	**82.1**	11.2	22.1	6.0	16.4	.000*

*P < 0.00001. ART-experienced participants had higher HRQOL dimensions and components compared with those of their ART-naïve counterparts. Using the t-test for independent samples, the values of P were less than 0.05 (significant) except for the CF and SE dimensions

Factors associated with Depression and HRQOL in HIV-infected persons

By multiple linear regression using SPSS, independent variables of age, sex, education, marital status, employment status, symptoms, CD4 count and duration since HIV was diagnosed were regressed against depression scores and HRQOL components of MHS and PHS. For each of the dependent variables, the model was stratified into ART-naïve and ART-experienced arms.

Table 4 shows that a male participant was expected to be 0.49 scores less depressed and to have 0.56 MHS scores higher than the female counterpart among ART-naïve clients when all other independent variables are held constant.

Table 4: MULTIPLE LINEAR REGRESSION COEFFICIENTS FOR DEPRESSION, MHS AND PHS SCORES

Variable	REGRESSION COEFFICIENTS					
	ART - Naive			ART - Experienced		
	CES-D	MHS	PHS	CES-D	MHS	PHS
Age (years)						
18-34	Ref	Ref	Ref	Ref	Ref	Ref
35-49	-0.057	0.068	-0.005	0.020	-0.052	-0.013
50-64	-0.002	-0.063	0.090	0.099	-0.094	0.010
Sex						
Female	Ref	Ref	Ref	Ref	Ref	Ref
Male	**-0.49*****	**0.565*****	0.140	-0.025	-0.188	0.126
Marital Status						
W/D/S	Ref	Ref	Ref	Ref	Ref	Ref
Single	**-0.136***	0.017	0.204	0.032	-0.051	0.108
Married	-0.121	-0.068	**0.264***	0.167	-0.175	-0.047
Education						
Pre-Secondary	Ref	Ref	Ref	Ref	Ref	Ref
Secondary	-0.048	-0.006	0.108	0.037	0.017	-0.175
Post-Secondary	-0.054	-0.069	0.162	0.002	-0.038	-0.013
Employment Status						
Unemployed	Ref	Ref	Ref	Ref	Ref	Ref
Employed	-0.349	0.335	0.085	-0.055	0.178	-0.016
Symptoms						
Symptomatic	Ref	Ref	Ref	Ref	Ref	Ref
Asymptomatic	-0.129	0.001	0.428	-0.015	-0.160	**0.250***
CD4 Count						
---	Ref	Ref	Ref	Ref	Ref	Ref
>350 Cells/ì L	0.013	0.047	-0.093	**-0.802*****	**0.895*****	**0.330****
HIV Duration						
<1 Year	Ref	Ref	Ref	Ref	Ref	Ref
>1 Year	0.107	-0.107	-0.072	0.072	-0.112	0.040

NB: Regression coefficients which are statistically significant (P < 0.05) are highlighted.
Ref: Means that particular category for the variable is a reference point.
W/D/S: Widowed / Divorced / Separated.
***P <0.001; ** P = 0.001-0.01; * P = 0.01-0.05

Single ART-naïve clients were expected to be 0.14 less depressed compared with their widowed, divorced or separated (W/D/S) counterparts assuming that all other variables were held constant. And married ART- naïve participants were 0.26 PHS scores higher than their W/D/S counterparts. Asymptomatic ART-experienced participants were expected to have 0.25 PHS scores higher than their symptomatic counterparts when all other independent variables are held constant. And ART-experienced participant with CD4 counts greater than 350 Cells/ì L were expected to be 0.80 scores less depressed but 0. 90 MHS scores and 0.33 PHS scores higher than

their counterpart with CD4 count less than 350 Cells/ì L when other independent variables are held constant.

DISCUSSION

The study demonstrated that ART-experienced adults had lower depression scores and higher HRQOL scores compared with their ART-naive HIV-infected counterparts at Mukinge Mission Hospital and Kasempa urban clinic. The study also showed that some independent variables were significantly associated with depression and HRQOL in these patients. These findings are consistent with prior cross sectional studies from other sub-Saharan African countries.

Most (66%) ART-experienced participants were on the first line regimen. One explanation for this could have been lack of access to routine viral load testing by which virologic failure could have been detected early enough to warrant switching to second line where necessary. Secondly, there could have been shortage of medical officers with the expertise to switch clients failing on first line to second line. There were more asymptomatic ART-experienced participants (80%) compared with the ART-naïve counterparts (60%). This is because ART reduces HIV-viral load resulting in improved immune system which leads to reduced opportunistic infections and hence less symptoms.

Many (74%) ART-experienced participants had CD4 counts $\geq$ 350 cells/ì L compared with their ART-naïve counterparts (39%). This happens because as ART reduces viral load there will be less viruses to infect the CD4 cells. Most (61%) ART-naive participants who had CD4 counts less than 350 cells/ì l had not yet been put on treatment because for many of them the interview took place on the actual day when they were booked to be commenced on ART.

From Figure 2 and Table 3, ART-experienced participants had higher scores in all dimensions of HRQOL and the MHS and PHS components compared with their counterparts. This could probably be attributed to self-stigmatization and self-condemnation among ART- naïve clients while coping with their HIV status in the first year of diagnosis as most of them (74%) were diagnosed with HIV within the previous one year. It may have been made worse by poor physical health as shown by symptoms in 40% of them compared with only 20% among ART-experienced participants

Male gender as opposed to female gender was associated with improvements in depression and MHS score among HIV-naïve participants (Table 4). This is what other studies have shown.[14,17] But among ART-experienced participants, gender difference did not cause any statistically significant changes in both depression and HRQOL.

Being single or married was associated with improvements in depression or in PHS component of HRQOL respectively among ART-naïve participants as shown even by other studies of studies. Marriage increases social support leading to improvements in depression and in HRQOL and the opposite is true in case of death or loss of a spouse. No significant changes were observed among ART-experienced participants in terms of marital status.

Being asymptomatic was associated with improvements in PHS scores among ART-experienced participants as observed even by other researchers.[21] ART leads to a reduction in the number of symptoms as explained earlier and this ultimately contributes to improve HRQOL. And finally, CD4 count $\geq$ 350 cells/ì L was associated significantly with improvements in depression, MHS and PHS scores among ART-experienced participants. An explanation for this could be that with higher CD4 counts, the immune system is improved and clients are able to fight opportunistic infections thereby improving their HRQOL. Age, education, employment status and duration with HIV diagnosis showed no significant association with depression and HRQOL in this study in both arms.

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