The association between depression and adherence to antiretroviral therapy in HIV-positive patients, KwaZulu-Natal, South Africa

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Abstract

Background: Depressive disorders are associated with poorer health outcomes in people living with human immunodeficiency virus infection and acquired immunodeficiency syndrome (PLHIV) and have been shown to contribute to non-adherence to antiretroviral therapy (ART) in Western contexts. Limited data from developing countries are available. The aim of this study was to explore whether there was an association between depressive symptoms and adherence to ART among PLHIV in KwaZulu-Natal, South Africa.

Method: A cross-sectional analytical study was undertaken in a population of HIV-positive patients accessing ART at a government funded, semi-urban clinic in the eThekwini Municipal District, KwaZulu-Natal, South Africa. The tools used to measure depressive symptoms and adherence were the Centre for Epidemiology Studies Depression Scale (CES-D) and clinic-based pill counts, respectively. Socio-demographic and clinical data were collected during interviews and from patient records.

Results: Sixty-two per cent of the sample (n = 146) had higher-than-threshold levels on the depression scale, and 32% were less than 95% adherent to ART. High depression scores were associated with lower levels of education [odds ratio (OR) 2.0; 95% confidence interval (CI), 1.0–4.1] and unemployment (OR 2.8; 95% CI, 1.3–6.0), while non-adherence was associated with unemployment (OR 2.4; 95% CI, 1.0–6.1) and mid-range CD4 counts (200–499 cells/µl; OR 3.0; 95% CI, 1.3–6.9). No significant association was found between depressive symptoms and non-adherence to ART (OR 0.5; 95% CI, 0.2–1.2; p-value, 0.125).

Conclusion: The large percentage of participants who scored high on the CES-D suggests a high prevalence of major depression in the study population. No significant association was found between high depression scores and non-adherence to ART. Depressive symptoms were significantly linked to lower levels of education and unemployment, while non-adherence was associated with unemployment and mid-range CD4 counts (200–499 cells/µl). The study had some limitations. Further studies are needed to determine the prevalence and causes of depression and its impact on PLHIV in this population and in the developing world.

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Introduction

Major depression, human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) contribute significantly to the global burden of disease, as indicated by the Global Burden of Disease study.[1] This study showed that HIV/AIDS and major depressive disorders were the third and fourth most important causes of disease burden in 2002. The authors estimate that HIV/AIDS will be ranked first and depression second by 2030.[1]

In Western countries, major depression has lifetime prevalence rates of around 15%.[2] According to a meta-analysis of 10 studies, this figure is nearly double in people living with HIV/AIDS (PLHIV).[3] The estimated prevalence of major depression was 9.7% among the general population in South Africa in 2004.[4] Few data are available on the prevalence of major depression and depressive disorders among PLHIV in the developing world. A study in Cape Town, South Africa, found the prevalence of major depression amongst PLHIV to be 14%,[5] while research from Stellenbosch showed prevalence rates of 34% on

presentation and 26% at follow-up.[6] These studies indicate a disparity in the prevalence of major depression, which could be related to the study population or to measurement tools. No prevalence data for major depression are available for PLHIV in KwaZulu-Natal, South Africa.

It is widely acknowledged that depressive disorders impact negatively on quality of life, mortality and adherence to medication among PLHIV.[7-9] In addition, mental illness increases the possibility of engaging in risky behaviour such as unprotected intercourse.[10]

Literature specific to PLHIV with depression in developing countries is sparse, and little is known about clinical and socio-demographic factors associated with depression in this context.[11] A Gambian study found that depressive symptoms were associated with a lack of income and a CD4 count of less than 200 cells/µl. In South Africa, among recently diagnosed PLHIV, depression was associated with female gender, disability and negative life events.[12] Depressive disorders among PLHIV were also thought to be related to the use of the antiretroviral drug efavirenz, but this was disputed by a large study in 2005.[13]

Optimal adherence to antiretroviral therapy (ART) is essential for viral suppression and positive treatment outcomes.[14] The negative impact of depressive disorders on adherence to ART has been demonstrated in developed countries.[9] There is evidence that the use of antidepressive medication leads to improved adherence.[15] Few studies have explored whether there is an association between depression and adherence to ART in Africa and specifically South Africa. Research conducted in KwaZulu-Natal among PLHIV attending three public hospitals showed that depression significantly increased the risk of non-adherence.[16] However, there is a lack of clinic-based data for South Africa despite the fact that the majority of people in this country access ART through clinic-based rather than hospital-based ART programmes.

There are other factors, apart from depression, that may adversely affect adherence to ART among South Africans with HIV/AIDS. These include a low CD4 count at the onset of ART, a relatively poor understanding of the disease and a lack of social support.[16] In addition, travelling costs, denial, waiting times at clinics, side effects of ART, use of traditional medicine, abuse of alcohol and being away from home have been identified as reasons for non-adherence in South Africa.[17]

Globally, psychiatrists advocate increased integration of mental health services into HIV/AIDS care.[18]

There is a paucity of local clinic-based data on depression and adherence to ART. The aim of this study was to explore whether there was any relationship between depressive symptoms and adherence to ART. The objectives of the study were (a) to screen for depression in a clinic-based sample, (b) to determine demographic and clinical associations with depressive symptoms, (c) to determine demographic and clinical associations with non-adherence to ART and (d) to establish whether there was an association between depressive symptoms and nonadherence to ART.

Method

Design and setting

This was a cross-sectional analytical study. The study was performed at a local government-funded ART clinic in a semi-urban isiZulu-speaking community on the outskirts of Durban, KwaZulu-Natal. About 1 420 patients are currently on ART at this clinic. Services provided at this clinic include counselling, nutritional assistance, psychosocial support and social welfare evaluation.

Sample and procedure

The required sample size of 151 participants was determined by a biostatistician. The calculated sample size made provision for age, gender, level of education, source of income, length of time on ART and CD4 count to be considered as confounders.

A convenience sampling method was employed. To meet inclusion criteria, participants had to be 18 years and older, able to provide written informed consent, have been on ART for six months or more and due for routine blood tests on the day of the interview [CD4 count and viral load (VL) as per National Department of Health guidelines]. Clinic attendees who had been on treatment for less than six months were purposefully excluded in order to minimise the potential effect of concurrent illness or adjustment disorders on their measured depression scores.

Questionnaires were translated into isiZulu by a qualified translator and back translated by counsellors from the clinic. A pilot study involving five clinic attendees was conducted to confirm that the isiZulu translation captured the meaning of the questionnaire.

Data were collected during a four-week period in October and November 2010. A trained and experienced isiZulu-speaking research assistant invited all patients who were waiting to have routine blood samples taken to be interviewed in private. The response rate was excellent with all participants who were approached agreeing to participate. Signed informed consents for interviews and for data to be collected from files were obtained. Overall, 160 interviews were conducted, of which 14 contained inadequate information or did not meet inclusion criteria. Therefore, 146 datasets were included in the analysis.

Approval was obtained from the Biomedical Research Ethics Committee and the Postgraduate Committee at the Nelson R Mandela School of Medicine, University of KwaZulu-Natal and the KwaZulu-Natal Provincial Department of Health.

Measuring instruments

Centre for Epidemiological Studies Depression Scale

The Centre for Epidemiological Studies Depression Scale (CES-D) was used to measure depressive symptoms. The CES-D has been translated into many languages and is used internationally in epidemiological studies and as a screening tool in clinical settings.[19] It is a 20-item scale that assesses current levels of depression as defined by Diagnostic and Statistical Manual of Mental Disorders IV criteria. Scores on the CES-D range from 0 to 60 with scores of 16 or more accepted as indicative of major depression. Participants are asked to rate the frequency of symptoms as a response to statements such as "I felt lonely", "I felt sad" and "I felt that my life had been a failure".

We chose to use the terms "significant depressive symptoms" and "CES-D-defined depression" for higher than threshold levels on the CES-D as no ideal brief measurement tool exists for major depression.[19] Valenstein et al. documented that studies conducted since 1995 report high sensitivities (81–100%) and moderate specificities (51–88%) for various screening instruments.[20] The CES-D has not been validated in the study population but has been validated in black undergraduate psychology students in South Africa.[21] A recent study in Cape Town among Afrikaans- and Xhosa-speaking PLHIV found the CES-D to have a sensitivity of 79% [95% confidence interval (CI): 76–83%] and a specificity of 61% (95% CI: 56–85%).[5]

The CES-D was chosen for this exploratory study because its wide use in epidemiological studies facilitates comparison among groups.[22] The brevity of the questionnaire and the fact that it can be administered by a lay person are important advantages over more robust measures of depression such as structured clinical interviews.[22] A further benefit in a setting where symptoms of depression and HIV-related illness often overlap is that it places less emphasis on physical manifestations of depression compared to other instruments such as the Beck Depression Inventory.[23] The CES-D is reported to demonstrate very high internal consistency, adequate test-retest reliability and good discriminant validity.[24]

For this study, the CES-D had a satisfactory internal consistency (Cronbach's alpha: 0.93).

Pill counting

Pill counting was used as measure of adherence. Pill counting has been validated as a reliable, replicable and economical tool to assess adherence in resource-poor settings.[25] Adherence is routinely assessed by pill counting at the clinic. Patients are required to bring all remaining tablets with them at follow-up visits. Tablets and number of days since last visit are counted and percentage adherence is calculated. The pill counting recorded on the day of the interview was used as measure of adherence.

Demographic and clinical data

The questionnaire included demographic data on gender, age, level of education and source of income. The researcher obtained clinical data (length of time on ART, treatment regime, previous CD4 count and VL, and current CD4 count and VL) from patient charts.

Data analysis

Data were analysed using Statistical Package for the Social Sciences™ version 18. Frequencies, means, standard deviations, median and inter-quartile range were calculated to describe the sample. Proportions and medians were compared using $\chi 2$ and Mann-Whitney U tests respectively.

Variables were entered into a logistic regression model if they displayed appreciable association in bivariate analysis ($p \leq 0.1$) or had theoretical importance. In the multivariate analysis, associations were considered significant at $p \leq 0.05$. Backward stepwise regression was applied, using the likelihood ratio statistic to determine the removal of variables for the final model. In order to facilitate reporting, categories found to be significant in the regression model were further collapsed and retested for significance.

Results

A total of 146 datasets was analysed. The results are summarised in Table I. The median age of participants was 36 years and the majority were female (62%).There were no reported differences in levels of education and employment status between male and female participants. Women were twice as likely to receive social grants compared to men (56% of women vs. 28% of men). Men were more likely than women to be dependent on family or friends for financial support (31% of men vs. 9% of women). Women had significantly higher median CD4 counts compared to men (346 cells/µl vs. 289cells/µl). The prevalence of CES-D-defined depression was high (62%). A third of the sample (32%) was less than 95% adherent to ART in the month prior to the interview.

In bivariate analysis, level of education (not having progressed further than primary school) and source of income (dependency on social grants or on family and friends) were significantly associated with depressive

Table I: Socio-demographic and clinical characteristics of the study sample (n = 146). P values are for the comparison between gender using $\chi 2$ tests for proportions and Mann-Whitney U tests for medians.

	Total		Male		Female		P value
	n = 146		n = 40		n = 106		
Median age in years ([a]IQR)	36	(31–42)	38	(33–42)	35	(31–42)	0.110
Level of education	n = 146		n = 40		n = 106		
None	7	(5%)	2	(52%)	5	(5%)	0.979
Primary	75	(51%)	20	(50%)	55	(5%)	
Higher and tertiary	64	(44%)	18	(45%)	46	(43%)	
Source of income	n = 146		n = 40		n = 106		
Employed	51	(35%)	16	(40%)	35	(33%)	0.002
Grant	73	(50%)	12	(30%)	61	(58%)	
Family	22	(15%)	12	(30%)	10	(9%)	
[b]ART	n = 146		n = 40		n = 106		
Median months on ART (IQR)	12	(6–25)	12	(6–19)	12	(6–25)	0.465
	n = 145		n = 40		n = 105		
Regimen with [c]EFV	116	(80%)	31	(78%)	85	(81%)	0.642
CD4 count (cells/µl)	n = 138		n = 39		n = 99		
0–199	37	(27%)	15	(39%)	22	(22%)	0.074
200–299	28	(20%)	7	(18%)	21	(21%)	
300–399	23	(17%)	6	(15%)	17	(17%)	
400–499	21	(15%)	8	(21%)	13	(13%)	
500 +	29	(21%)	3	(8%)	26	(26%)	
Median CD4 count (IQR)	312	(193–471)	289	(157–404)	346	(203–515)	0.039
Median change in CD4 from previous CD4 result (IQR)	98	(24–189)	69	(15–160)	107	(37–197)	0.195
[d]VL (copies/ml)	n = 130		n = 36		n = 94		0.462
Detectable (≥ 40)	27	(21%)	9	(25%)	18	(19%)	
Adherence	n = 142		n = 39		n = 103		
Non-adherent (< 95%)	45	(32%)	11	(28%)	34	(33%)	0.583
Depressive symptoms	n = 146		n = 40		n = 106		
[e]CES-D score ≥ 16 (on a scale 0-60)	91	(62%)	23	(58%)	68	(64%)	0.459
Median CES-D score (IQR)	27	(6–41)	21	(4–38)	27	(6–42)	0.334

a= interquartile range; b= antiretroviral therapy; c= efavirenz; d= viral load
e= Centres for Epidemiological Studies Depression Scale

symptoms. Source of income (dependency on family and friends) and CD4 count were significantly associated with non-adherence to ART.

Table II demonstrates significant associations with depressive symptoms in multivariate analysis. Unemployed participants were nearly three times more likely to be depressed [odds ratio (OR) 2.8; 95% CI, 1.3–6] than employed participants. Clinic attendees with primary school as highest level of education were twice more likely to score high on the depression scale than their more educated counterparts (OR 2; 95% CI, 1.0–4.1). There were no significant associations between depressive symptoms and clinical variables.

Unemployment was the only socio-demographic factor associated with non-adherence in multivariate analysis. Unemployed participants were twice more likely to be non-adherent than employed participants (OR 2.4; 95% CI, 1.0–6.1). The clinical variable associated with non-adherence was CD4 count. Participants with CD4 counts of 200–499 cells/µl were three times more likely to be non-adherent than those with higher or lower CD4 counts (OR 3; 95% CI, 1.3–6.9).

No significant association was found between CES-D-defined depression and non-adherence to ART (OR 0.5; 95% CI, 0.2–1.2; p=0.125).

Table II: Results of a multivariate logistic regression on depressive symptoms and non-adherence

	P value	[a]OR	95% [b]CI for OR
Associations with depressive symptoms (n = 145)			
Education up to primary school	**0.068**	2.0	1.0–4.1
Unemployed	**0.006**	2.8	1.3–6.0
Associations with non-adherence (n = 133)			
Symptoms of depression	0.125	0.5	0.2–1.2
Unemployed	**0.063**	2.4	1.0–6.1
Mid-range CD4 count (200–499)	**0.009**	3.0	1.3–6.9

a= odds ratio
b= confidence interval

Discussion

The prevalence of depression varies greatly among different populations.[11] This variability could be due to the use of different measures and methodologies or to differing study populations. The findings from this study are consistent with those of similar studies with the CES-D as measurement tool.[26-28] In this study, 62% of participants scored high on the CES-D. The large percentage of participants with significant depressive symptoms suggests that there is a very high prevalence of major depression in this HIV-positive population.

This large proportion of participants with high depression scores may reflect a high burden of psychological distress linked to poverty. The findings from this study regarding the increased risk of significant depressive symptoms among the unemployed and among people with lower levels of education have been confirmed by studies from both middle- and low-income countries.[29, 30]

It may be assumed that physically unwell PLHIV are likely to be more depressed than their healthy counterparts. However, a meta-analysis of 10 studies investigating the relationship between HIV infection and the risk for depressive disorders found that rates of depression were not linked to the disease stage of individuals with HIV.[31] This study did not find a significant association between CD4 count (as proxy of wellness) and depressive symptoms.

It is of concern that 32% of participants were less than 95% adherent to ART. These adherence rates are similar to those of a study in KwaZulu-Natal using different measuring instruments.[16] Unemployment has been linked to poor adherence to ART in this study and in another South African setting.[32] These findings are not surprising as lack of finances is an enormous barrier to adherence in the African context.[33]

The increased risk of non-adherence among participants with CD4 counts between 200 cells/µl and 499 cells/µl is noteworthy. It is plausible that our results reflect complacency towards adherence among participants with mid-range CD4 counts. Patients who are aware that they have very low CD4 counts (less than 200 cells/µl), however, may be more motivated to be adherent to ART. It stands to reason that good adherence results in high CD4 counts (over 500 cells/µl). A literature search rendered no current evidence supporting this suggestion.

It is of interest that there was no significant association between the relatively high prevalence of significant depressive symptoms and non-adherence to ART. It is possible that factors such as self-efficacy,[34] the ability to express emotions,[35] differing cultural expressions of psychological distress[36] and complex adherence behaviour[37] influenced results. Another reason could be that few other studies exploring the risk of non-adherence in depressed patients have excluded participants who recently started ART. It has been shown in other populations that adherence improves over time[38] while depression may persist.[12] The likelihood that these phenomena were captured in our results needs to be considered in future research.

This study has a number of limitations. First, the CES-D has not been validated in this population. In general, brief rating scales for depression lack specificity. Second, pill counting as measure of adherence is not without problems as it does not account for events such as the sharing or losing of tablets or patients throwing remaining tablets away in order to appear adherent. Third, the response rate was excellent, but the study sample may not have been representative of the study population as a convenience sampling method was employed. Fourth, all potential confounding factors, such as recent bereavement, alcoholism, major life events, social support, stigma and previous history of depression were not taken into account in the analysis. Fifth, the cross-sectional design does not allow for conclusions to be drawn regarding temporal relationships between adherence and depressive symptoms. In light of the limitations, caution should be taken in generalising findings to other districts in South Africa.

Conclusion and recommendations

Research in Western contexts indicates a high prevalence of depression in PLHIV. It has also been shown that depressive disorders jeopardise the health outcomes of patients with HIV. Literature from the developing world on depression in PLHIV is limited.

Brief rating scales for depression, though widely used, are not ideal diagnostic tools as they lack specificity. However, the large percentage of participants with significant depressive symptoms suggests that there is a high prevalence of major

depression in the study population. This study did not find a significant relationship between depressive symptoms and non-adherence to ART.

Participants with significant depressive symptoms were more likely to be unemployed and to have lower levels of education. Unemployed participants and those with mid-range CD4 counts (200–499 cells/µl) were at increased risk of non-adherence to ART. Healthcare workers should be aware of the fact that these groups of patients are likely to require additional support.

Further studies using robust diagnostic tools are recommended to determine the prevalence, causes and impact of depression among PLHIV in South Africa and in the developing world.

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