

Adherence to highly active antiretroviral therapy in depressed patients with HIV/AIDS attending a Nigerian university teaching hospital clinic

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Abstract

Objective: To determine the prevalence of depressive disorder in patients with HIV/AIDS receiving HAART; to determine the effect of depressive disorder on adherence to antiretroviral therapy; and to determine the significance of the association.

Method: The study was conducted amongst outpatients of Ahmadu Bello University Teaching Hospital, Zaria. A socio-demographic and drug adherence questionnaire was administered. The Centre for Epidemiological Studies Depression Scale (CES-D) was used to screen for depressive symptoms while the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) was used to confirm the diagnosis of depressive disorder. **Results:** A total of 310 patients with HIV/AIDS receiving HAART participated in the study. 68.4% were female and the mean age was 35.5 (\pm 8.97 years). 37.4% had secondary education, while 27.1% had tertiary education. Sixty-six participants (21.3%) had significant depressive symptoms while 14.2% met ICD-10 diagnostic criteria for depressive disorder. Overall, 73% of participants had good adherence to HAART. 63.6% of participants with depressive disorder had poor adherence to HAART compared to 21.1% of participants without depressive disorder ($p < 0.05$).

Conclusion: Depressive disorder in patients with HIV/AIDS is associated with poor adherence to antiretroviral medication. Early identification and treatment of depression in such patients may improve antiretroviral medication adherence and treatment outcomes.

Key words: Medication adherence; Depressive disorder; Highly Active Antiretroviral Therapy; HIV infection.

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Introduction

The most recent statistics on the global epidemic of HIV/AIDS indicates that 39.5 million people are living with HIV/AIDS worldwide. Of these, 24.7 million (63%) live in Sub-Saharan Africa, a region that is home to just 10% of the world's population.¹ Nigeria has the third largest population

of people living with HIV/AIDS in the world, after India and South Africa. The seroprevalence rate increased from 1.8% in 1991 to 5.8% in 2001, with only a modest drop to 4.4% in 2005.²

Treatment for HIV/AIDS is accomplished through numerous combinations of antiretroviral agents belonging to the following groups: Nucleoside analogue reverse transcriptase inhibitors, nonnucleoside reverse transcriptase inhibitors and protease inhibitors. In the mid-1990s, several investigators studied combination therapies of two reverse transcriptase inhibitors and a protease inhibitor. This therapy was later referred to as Highly Active Antiretroviral Therapy

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(HAART). HAART dramatically reduces viral load,³ and the goal of treatment is to reduce viral load to undetectable levels and maintain such remission without interruption. Evidence suggests that these therapies suppress replication but do not eradicate HIV from all parts of the body. Not all patients who initiate antiretroviral therapy respond. The lack of clinical response is likely explained by problems with adherence, suboptimal antiretroviral treatment potency, and genetic mutation of HIV strains.⁴

Adherence to antiretroviral therapy (ART) is of critical importance because even minor deviations from the prescribed regimen can result in viral resistance.^{5,6} Studies of ART continue to indicate that a near-perfect adherence is required to adequately repress viral replication.^{7,8} Adherence can be measured in several ways such as counting prescriptions filled (pill counting), care givers' reports, drug-blood level monitoring and self report by patients. Multiple factors influence adherence among patients with HIV/AIDS. Such factors include patients' age, regimen complexity, drug side-effects, advanced HIV disease and patients' mental health.⁹ Other factors include unfamiliarity with the implications of having a chronic, potentially deadly disease, the complex impact of ART on interpersonal relationships, depression and hopelessness, lack of accurate information, and issues related to local cultural frameworks (e.g. illness ideology).¹⁰ A Ugandan study showed that adherence to ART declined over time and that factors such as lack of transportation and money, stigma, clinical response to therapy, drug packaging and cost may impact on adherence.¹¹ Long-term viral suppression requires consistent and high percentage adherence accompanied by optimal inter-dose intervals. Efforts to improve viral outcomes should address not only missed doses but wide variations in dose timing.¹²

HIV infection can lead to neuropsychiatric syndromes.¹³ Clinicians need to be aware of this possibility when evaluating new patients and observing changes in patients whom they treat.¹⁴ Depression is the most commonly observed psychiatric disorder among patients with HIV infection.¹⁵⁻¹⁸ The prevalence rate of depression in HIV-positive clinic populations ranges from 22 to 32% which is about 3 to 5 times higher than that in the general population.^{19,20} Importantly, this may be an underestimation as there is evidence that depression may be under-diagnosed in the context of HIV medical care.²¹ HIV increases the risk of developing major depression through a variety of mechanisms including: direct injury to subcortical areas of the brain; chronic stress; stigmatization; worsening social isolation; bereavement; debilitation; and intense demoralization.²²

Research suggests that co-morbid depression in patients with HIV/AIDS may be associated with reduced adherence to ART^{11,23-27} and furthermore with disease progression.^{28,29} A study in Ethiopia found that patients who were not depressed were two times more likely to be adherent than those who were depressed, although the principal reasons given for skipping doses were simply forgetting, feeling ill, being busy and running out of medication. These authors concluded that adherence is a dynamic process which changes over time and cannot reliably be predicted by a few patients' characteristics that

are assumed to vary with time.³⁰ A further study in Tanzania showed that self-reported adherence was high in HIV-positive patients on ART despite economic hardship, depression, low rates of HIV disclosure and high perceived HIV-associated stigma.³¹ The authors cited the following factors as key to improving adherence to ART: substantial improvement in health condition after starting ART; perceived need to meet family responsibilities; development of specific strategies to remember to take pills; material/emotional support received from others; and regular advice/instruction from health care providers emphasizing adherence. There is further evidence for additional motivating factors such as the values of church involvement and marriage.¹⁰

The rationale for this study is based on the observation by physicians caring for patients with HIV/AIDS that a significant proportion of patients in treatment have poor adherence to ART despite adequate exposure to medication adherence counselling. It is highly relevant therefore to investigate possible factors contributing to non-adherence. The aim of this study was to determine the prevalence of depressive disorder in patients with HIV/AIDS and to study its effect on adherence to antiretroviral medication.

Method

The participants consisted of a consecutive sample of 310 patients with HIV/AIDS attending the virology clinic at the Ahmadu Bello University Teaching Hospital, Zaria during the period from September to December 2006 who gave informed consent and met the inclusion criteria for the study. Eligibility criteria included patients with confirmed HIV infection on ART. Exclusion criteria included: those patients who were known to have other comorbid chronic medical conditions; patients known to have other psychiatric conditions besides depression; and those found to have marked cognitive impairment. To assess for cognitive impairment, all participants in the study were initially screened by the same investigator for cognitive impairment by carrying out a mental state examination. They were assessed for recent memory, remote memory and orientation in person, place and time. Participants found to have impaired memory and disorientation in person, place or time were excluded from the study. Ethical clearance for the study was obtained from the Research and Ethics Committee of the hospital.

Participants in the study completed the sociodemographic and adherence questionnaires. The former gathered information on age, gender, marital status, education and occupation. Occupation was classified using the method described by Borroffka and Olatawura.³² The adherence questionnaire obtained information about missed doses of antiretroviral drugs during the past week, reasons for poor adherence and the number of antiretroviral pills not used at the appropriate inter-dose intervals in the past week. Poor adherence was defined as the subject's self-report of having missed any dose of antiretroviral medications over the previous 7 days while the drugs were available.

All participants were screened for depressive symptoms using the Center for Epidemiologic Studies Depression

Scale, Revised (CES-DR). Those with a CES-DR score of 16 and above were considered to have significant depressive symptoms³³ and were administered the relevant sections of the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) <http://epi.wustl.edu/epi/assessments/scan.htm>. Thirty participants (about 10% of the sample) who slightly fell short of attaining the CES-DR cut off score of 16 were randomly selected and also administered the SCAN. The Research Diagnostic Criteria (RDC) of the International Classification of Diseases (ICD-10)³⁴ was used to generate a clinical diagnosis of depressive disorder based on depressive symptoms elicited with the SCAN. All the participants completed the assessment.

The twelfth edition of the Statistical Package for Social Sciences (SPSS-12) software was used for data analysis. Data was analysed by means of descriptive statistics. These included frequencies, percentages, means and standard deviation. The chi-square test was used to characterise the significance of the difference between ART adherence in depressed HIV/AIDS patients compared to non-depressed HIV/AIDS patients. The level of significance was set at 5% confidence limit.

Results

A total of 310 subjects with HIV/AIDS participated in the study. The mean duration of illness was 26.5 (SD 8.9) months and the

mean duration of antiretroviral drug treatment was 17.7 (SD 5.2) months.

The socio-demographic characteristics of participants are presented in Table 1.

Sixty-six participants (21.3%) had significant depressive symptoms (CES-DR score ≥ 16), while forty-four (14.2%) met diagnostic criteria for depressive disorder based on the Research Diagnostic Criteria (RDC). Kappa statistics between those identified depressed by CESD-DR and ICD-10 criteria was 0.759 signifying a good agreement. Socio-demographic characteristics (age, sex, education and occupation) did not differ significantly between participants with depressive disorder and those without depressive disorder.

In the total sample, eighty-four participants (27%) had poor adherence to HAART. Table II presents the reasons given for poor adherence as well as the number of pills used with wide variation in inter-dose timing by participants with and without depressive disorder.

Table II: Reasons for poor medication adherence, and the number of pills used with wide variations in inter-dose timing by participants with and without ICD-10 diagnosis of depressive disorder

Reasons for missing pills	Depressive disorder	No Depressive disorder
Forgot	14 (53.8%)	45 (77.6%)
Drugs not available	0 (0%)	2 (3.4%)
I got tired of them	11 (42.3%)	6 (10.3%)
Others (travelled, fasting)	1 (3.8%)	5 (8.6%)
Total	26 (100%)	58 (100%) n= 84
<i>Number of pills not used on time in the past week</i>		
0	7 (15.9%)	69 (25.94%)
1 to 9	24 (54.54%)	174 (65.41%)
10 and above	13 (29.54%)	23 (8.65%)
Total	44 (100%)	266 (100%) n= 310
$\chi^2 = 16.447, df = 2, p < 0.05$		

Finally, ART adherence in participants with depressive disorder (36.4%) was significantly poorer than that in non-depressed participants (78.9%) ($p < 0.05$). These results are shown in Table III.

Table III: Adherence to antiretroviral medication by participants with and without ICD-10 diagnosis of depression

Adherence	Depressive disorder	No Depressive disorder	Total
Poor Adherence	28 (63.6%)	56 (21.1%)	84
Good Adherence	16 (36.4%)	210 (78.9%)	226
Total	44 (100%)	266 (100%)	310
$\chi^2 = 34.657, df = 1, p < 0.05$			

Table I: Socio-demographic characteristics of participants		
Variable	Frequency	Percentage
Gender		
Male	98	31.6
Female	212	68.4
Mean age overall	35.5 (SD 8.97) years	(t = 6.32; p < 0.05)
Mean age males	40.10 (8.8) years	
Mean age females	33.42 (8.2) years	
Religion		
Islam	124	40
Christianity	186	60
Marital status		
Single	66	21.3
Married	164	52.9
Divorced	14	4.5
Widowed	64	20.6
Separated	2	0.6
Occupation		
Unemployed	120	38.7
Unskilled worker	29	9.4
Petty trader	48	15.5
Semiskilled worker	22	7.1
Highly skilled professional	85	27.4
Retired	6	1.9
Education		
Primary	62	20
Secondary	116	37.4
Tertiary	84	27.1
Arabic	20	6.5
None	28	9.0

Discussion

This study found a female preponderance (68.4%) among patients with HIV/AIDS. This is consistent with the UNAIDS/WHO global report¹, which stated that unlike women in other regions of the world, African women are considerably more likely – at least 1.4 times – to be infected with HIV than men. In this study, possible explanations for the female preponderance is that women, especially those of child-bearing age, are more likely to have their HIV disease detected either through routine screening in the antenatal clinics or when their babies develop HIV-associated illnesses shortly after birth. A number of other studies also report a female preponderance.¹⁷

The mean age of participants was 35.53 (SD 8.9) years. This reflects the fact that people are most sexually active between the ages of 18 and 25 years and are likely to acquire the infection during this period. However, symptoms may not become apparent until roughly 10 to 12 years after initial infection, making it more likely for patients to present in their 30s. Some previous studies also had similar findings.¹⁷ In the current study, the mean age for females was significantly lower than for males. This may be because they are more likely to engage in sexual experiences earlier than males since they attain sexual maturity earlier. Also, older men may be more likely to engage in sexual acts with much younger women. A large proportion of participants in this study was unemployed (38.7%) as is the case in many other studies.¹⁸ This may be due to ill-health and discrimination. Also, there is a relationship between poverty and disease. Highly skilled professionals constituted 27.4% of the sample and this may reflect the cosmopolitan nature of the population and the fact that highly skilled professionals may be more likely to get health information and present for treatment. For similar reasons, the majority of the participants had some or had completed secondary and tertiary education.

Most of the people living with HIV/AIDS in this study had a short illness and treatment duration. This may be a reflection of the recent efforts in the country by government, non-governmental organizations and international agencies aimed at promoting voluntary counselling and testing, public enlightenment about HIV/AIDS, and free ART for people infected with HIV.

A significant proportion of the participants had depressive symptoms and 14.2% had depressive disorder. This is in keeping with several other studies that found an increased prevalence of depressive disorder in HIV-positive clinic populations.³⁵ However it is somewhat lower than rates reported in other studies (22%¹⁹ and 32%²⁰). This may be due to differences in the study population and the ascertainment tools or methodology used. Depression in HIV patients is due to a combination of factors which include the effects of the virus on the subcortical areas of the brain, chronic stress resulting from unemployment, poor financial security, burden of care for the disease, stigmatization, bereavement and intense demoralization.

Our finding that 27% of all participants had poor adherence is consistent with findings in some other studies.^{26,36} The participants gave various reasons for poor adherence to ART. A large proportion of participants with depressive disorder (42.3%) said they did not use their medication regularly because they got tired of them.

Depression can produce cognitive impairment, as depressed subjects have been found to have impaired attention, concentration and memory. In severe cases, they may have a dementia-like syndrome (pseudo-dementia). The consequence is that depressed patients with HIV/AIDS may be more likely to forget using their pills leading to poor medication adherence. HIV-infected subjects in several studies³⁰ reported "forgetting" as one of the most common reasons for poor adherence to antiretroviral drugs. It is also possible that HIV-associated neurocognitive disturbances, which are common and more prominent as the disease advances, might be responsible for some of the cases of poor medication adherence reported in this study. Other studies have reported a significantly greater risk of poor adherence to HAART in HIV-infected persons with neurocognitive impairment.³⁷

Previous studies have shown that long-term viral suppression requires consistent adherence accompanied by optimal inter-dose intervals. This study found that 29.54% of the participants with depressive disorder did not use (at the right time) ten or more antiretroviral pills in the previous week, compared to only 8.65% in patients without depression. Also, the significant association between depressive disorder and poor adherence suggests that depression is associated with poor medication adherence. This was the case both in terms of missed doses and in terms of wide variations in inter-dose timing ($p < 0.05$). Our finding is consistent with that of some other studies.^{11,24-27} The expression of depressive symptoms such as loss of interest, hopelessness, lack of energy, poor concentration and memory seen in depressive disorders is likely to have contributed to poor adherence to ART in the depressed participants.

Limitations

There are some limitations in this study. Participants were asked to recall use of medicines and some may have given incorrect answers due to problems with memory. Furthermore, assessment of cognitive functioning in this study using the mental state examination was rather subjective. A more objective assessment of cognition with an instrument such as the Mini Mental State Examination is recommended to effectively identify participants with cognitive impairment and to measure severity. Finally, the study was hospital based and may not reflect what goes on in the community. However, we have reported information on those who approach medical facilities for treatment, yet still do not comply with treatment because of unrecognized depression.

Conclusion

There is the need to design interventions that will enhance early identification and treatment of depression in patients with HIV/AIDS, especially in those whose medication adherence fails to improve after adequate general measures. Such interventions may include the training of physicians in the use of depression screening instruments during their routine HIV/AIDS patient care. This would improve case identification and, ultimately, would positively impact on treatment and outcome through improving antiretroviral medication adherence.

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