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Depression and CD4 Cell Count Among Persons with HIV Infection in Uganda

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Abstract Despite the importance of mental illness and the high prevalence of HIV in Africa, few studies have documented depressive symptoms among HIV-infected persons in Africa. We assessed factors associated with depression among HIV-infected adults undergoing anti-retroviral eligibility screening in Eastern Uganda. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CES-D). Univariate and multiple regression analyses were conducted to identify socio-demographic characteristics and disease-related factors associated with depression. Among 1017 HIV-infected participants assessed for depression, 47% (476/1017) reported depressive symptoms (CES-D ≥ 23). Adjusting for age, gender, education, and source of income, patients with CD4 counts < 50 cells/μl were more likely to be depressed (odds ratio 2.34, 95% confidence interval, 1.39–3.93, $P = 0.001$). Women, participants >50 years, and those without an income source were more likely to be depressed. Depression was common among HIV-infected persons in rural Uganda and was associated with low CD4 cell counts. Appropriate screening and treatment for depression should be considered for comprehensive HIV care.

Keywords Depression · HIV/AIDS · CD4 cell count · CES-D depression scale · Africa · Uganda

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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Introduction

The prevalence of depression among persons with HIV/AIDS in industrialized countries is high, ranging from 9 to 60% (Burack et al., 1993; Ciesla & Roberts, 2001; Cook et al., 2004; Lyketsos et al., 1996b; Moneyham, Sowell, Seals, & Demi, 2000; Moore et al., 1999; Richardson et al., 2001), and persons with HIV in these settings have nearly twice the risk of developing major depressive disorder compared with HIV-negative persons (Ciesla & Roberts, 2001). Factors associated with depressive symptoms among HIV-infected adults in industrialized

countries include number of HIV-related symptoms, income, ethnicity, drug and alcohol use, domestic violence, AIDS-defining illness, gender, education and age (Moore et al., 1999; Richardson et al., 2001). In Africa, where the majority of people with HIV live (UNAIDS, 2004), less is known about the prevalence of depressive symptoms among persons with HIV (Bolton, Wilk, &Ndogoni, 2004; Maj et al., 1991) and the socio-demographic and HIV-related factors associated with depression. Among recently diagnosed HIV patients in South Africa, the prevalence of major depression was found to be 35% (Olley et al., 2003) and gender, negative life events and disability were associated with current major depression (Olley, Seedat, Nei, &Stein, 2004). However, a study conducted among a random sample of adults living in a high HIV prevalence area in rural Southwest Uganda found increased age and lower educational levels, but not gender, to be associated with depression (Bolton et al., 2004).

Depression is of particular concern for HIV-infected persons because it is correlated with accelerated HIV disease progression (Leserman et al., 1999; Page-Shafer, Delorenze, Satariano, & Winkelstein, 1996; Ickovics et al., 2001). However, diagnosis and treatment for depression is currently not available in much of Africa. While antidepressants are expensive and not widely available in Uganda, a study using group interpersonal psychotherapy sessions improved psychological well-being among depressed people in rural Uganda (Bolton et al., 2003). However, this intervention trial was conducted in the general population; less is known about how to address depression among HIV-infected persons in Africa.

Identifying depression within HIV-infected populations in Africa could be an important step towards developing interventions that reduce depression in HIV-infected persons. While previous studies suggest that the socio-demographic factors associated with depression in Africa may be similar to those in industrialized countries, it is unclear how clinical indicators of disease severity are associated with the prevalence of depression among persons infected with HIV. Within AIDS care and treatment programs in Africa, CD4 cell count testing is increasingly being used for clinical management and thus clinical markers may be more readily available in patient records than social factors. To better understand the relationship between socio-demographic factors, CD4 cell count and depressive symptoms, we conducted a cross-sectional analysis among 1017 persons with HIV who were screened for antiretroviral therapy (ART) in rural Uganda.

Methods

Study Population

We analyzed data from 1017 HIV-infected adults who were screened for enrolment in the Home-based AIDS Care Project (HBAC), a 3-year randomized trial designed to examine three different ways to clinically monitor ART in rural Uganda. The enrollment procedures have been previously described (Bunnell et al., 2006) and are briefly summarized here. Between May 2003 and May 2004, 2,097 HIV-1 infected adults were screened to assess eligibility for ART from Tororo, Busia, Mbale and Bugiri districts in Northeastern Uganda. Potential participants were clients of the Tororo branch of The AIDS Support Organization (TASO), a non-governmental organization that has provided HIV/AIDS care and support since 1987. Membership is open to any HIV-infected person free-of-charge. TASO's membership is nearly 70% female, probably as a result of higher HIV prevalence among women and of gender-based differences in health-seeking behaviors in Uganda. Persons were included in this depression analysis if they (1) were clinically eligible for ART, (2) had completed a depression assessment prior to knowing the outcome of their ART eligibility screening, (3) were ART naïve, and (4) had not originally enrolled as a household member of another participant in the study.

Procedures

Research counselors, trained in rapport-building techniques and approaches for eliciting information on sensitive topics, conducted structured interviews with participants in a neutral, non-judgmental manner using questionnaires translated into six local languages. Interviewers and participants were matched by ethnic background. During screening, participants were interviewed regarding demographic characteristics and presence of depressive symptoms using a standardized questionnaire. Blood samples were drawn to confirm HIV status and assess CD4 cell count (if HIV positive). Only HIV-positive participants who underwent assessments for depression prior to knowing the outcome of their ART eligibility screening were included in the current analysis. This study was approved by the Science and Ethics Committee of the Uganda Virus Research Institute, the Uganda National Council of Science and Technology, and the Institutional Review Boards of the Centers for Disease Control and Prevention (CDC) and the University of California, San Francisco. Funding was provided by Department of

Health and Human Services through the President's Emergency Plan for AIDS Relief.

Measures

Depressive Symptoms

Depressive symptoms were measured using the Center for Epidemiological Studies Depression scale (CES-D), a 20-item self-report scale that assesses the frequency of depressive symptoms over the previous seven days (Radloff, 1977). The CES-D is often used to measure depressive symptoms in population-based research and has been validated among a variety of study populations in both developed (Myers & Weissman, 1980; Radloff, 1977) and developing countries (Cheng & Chan, 2005; Yang, Soong, Kuo, Chang, & Chen, 2004). Study participants reported the frequency of occurrence of each item in the past 7 days on a scale of 0 (rarely or none of the time) to 3 (most or all of the time). Appropriate items were reverse-coded and summed to compute a total score ranging from 0 to 60, with higher scores indicating more depressive symptoms. Since we did not have a clinical diagnosis of depression but only depressive symptomatology, we assessed the distribution of CES-D scores across a 3-level categorization for depression, with <16 being not depressed, 16–22 being ''distressed'' and >23 being depressed (Mills et al., 2004). For the analysis of factors associated with depression, a cut-off of 23 was used to define 'probable cases of depression'.

In addition, a modified depression scale was computed by removing the CES-D items reflecting somatic complaints and items that did not represent symptoms of depression in this population and other HIV-infected populations (Kalichman, Rompa, & Cage, 2000). From factor analysis, somatic items included feeling things were an effort, trouble with attention, not able to ''get going,'' and feeling depressed (factor loadings >0.46). Items that did not reflect depression included feeling bothered, appetite loss, restless sleep, and not feeling as good as others (factor loadings <0.40). The remaining 12 items were reverse-coded where appropriate and summed to compute a total score that could range from 0 to 36. The modified scale was internally consistent (alpha = 0.85) with a mean of 11.4 (SD = 7.7). A cutoff of 14 or higher was used to define a dichotomous 'depression' variable on this scale. The cutoff on the modified scale was chosen to be proportionate to a score of 23 on the full CESD scale.

HIV-Related Clinical Measures

For all HIV-positive participants screened, CD4 cell count was measured using TriTEST reagents following an in-house, dual platform protocol and MultiSET and Attractors software using a FACScan flow cytometer (Becton-Dickinson, NJ, USA).

Socio-demographic Characteristics

Demographic factors collected included gender, age, religion, main source of income, education, marital status, and number of living children. For the income variable, 'trade' included all forms of activity that created an income, 'salary' included wage and salaried employment, 'farming' consisted of agricultural farming and 'dependent' included those who reported receiving money from others as their main source of income. Due to the small number of single participants screened, single and widowed participants were combined into one category.

Data Analysis

Data were double-entered in Epi-Info 2004 and analyzed using SAS/STAT® software, version 9.0. Factor analysis was conducted to examine the underlying factor structure of the CES-D items using principal component analysis with varimax rotation. Cronbach's alpha values were calculated for all sub-scales and the overall scale to assess internal consistency reliability. Construct validity was examined by comparing the significant unadjusted associations observed with those reported in previous validation studies in other populations. Univariate and multiple logistic regression analyses were conducted to examine the unadjusted and adjusted associations of potential risk factors and depressive symptoms, respectively. Factors that were significant in univariate analyses at the $p < 0.05$ level were included in a multivariate model.

Results

Participant Characteristics

We assessed 1225 adults for participation before they knew their ART eligibility status. Of these, 29 were HIV-negative, 60 did not complete the medical or interview process, and five died during the screening period. Of the remaining 1131 participants, data were excluded from 43 (4%) who reported

prior ART use and 71 (6%) who lived with a household member receiving ART at the time of screening. Thus, 1017 participants were included in the current analysis.

The mean age of participants was 38 years for females and 42 years for males. The majority of participants were female, widowed, had completed primary education, and had a CD4 cell count greater than 200 cells/μl. Twenty-two percent had a CD4 cell count less than 100 cells/μl (see Table 1).

Prevalence and Factors Associated with Depressive Symptoms

Overall, the prevalence of depressive symptoms, defined as a CESD score ≥23, was 47%. Only 19% of the participants had a CESD score between 16 and 22 indicating a ''distressed'' state, and 34% had a score below 16, indicating no depression. In univariate analysis, presence of depressive symptoms was associated with female gender, older age, low or no source of

Table 1 Prevalence and potential risk factors of depressive symptoms among HIV-infected adults in rural Uganda

Potential risk factor		CESD Score		Association with depressive symptoms (CESD ≥ 23)	
	Total N = 1017 (%)	<23	≥23	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
Overall	1017	53%	47%		
Sex					
Men	236 (23)	60	40	1.00	1.00
Women	781 (77)	51	49	1.44 (1.08, 1.94)	1.62 (1.13, 2.31)**
Age					
18–30 years	180 (18)	58	42	1.00	1.00
31–40 years	452 (44)	54	46	1.15 (0.80, 1.62)	1.21 (0.83, 1.74)
41–50 years	291 (29)	51	49	1.30 (0.90, 1.90)	1.42 (0.93, 2.17)
>50 years	94 (9)	45	55	1.69 (1.02, 2.80)	1.93 (1.09, 3.42)**
Religion					
Catholic	469 (46)	51	49	1.00	
Muslim	27 (3)	56	44	0.84 (0.39, 1.84)	
Fundamentalist	174 (17)	56	44	0.84 (0.59, 1.19)	
Protestant	346 (34)	54	46	0.88 (0.67, 1.17)	
Main source of income[b]					
Trade	291 (29)	59	41	1.00	1.00
Salary	152 (15)	57	43	1.11 (0.75, 1.65)	1.13 (0.75, 1.72)
Farming	375 (37)	54	46	1.25 (0.92, 1.71)	1.26 (0.91, 1.75)
Pensions	199 (20)	41	59	2.06 (1.43, 2.98)	1.81 (1.24, 2.66)**
Education					
Post-primary	216 (21)	45	55	1.00	1.00
Primary	559 (55)	55	45	1.19 (0.86, 1.63)	1.69 (1.12, −2.52)*
None	242 (24)	59	41	1.74 (1.20, 2.52)	1.31 (0.93, −1.84)
Marital status					
Married/co-habiting	378 (37)	56	44	1.00	
Divorced/separated	98 (10)	46	54	1.47 (0.94, 2.30)	
Widowed/single	541 (53)	53	47	1.11 (0.86, 1.45)	
Number of living children					
0–1	122 (12)	53	47	1.00	
2–4	465 (48)	53	47	0.98 (0.66, 1.46)	
≥5	430 (42)	54	46	0.95 (0.64, 1.42)	
*CD4 count (cells/*μl)					
≥500	159 (16)	40	60	1.00	1.00
200–499	399 (39)	42	58	1.10 (0.76, 1.60)	1.05 (0.71, 1.54)
100–199	234 (23)	53	47	1.35 (0.90, 2.03)	1.32 (0.87, 2.02)
50–99	111 (11)	58	42	2.04 (1.25, 3.34)	2.02 (1.22, 3.36)**
<50	113 (11)	60	40	2.27 (1.39, 3.71)	2.34 (1.39, 3.93)***

OR, odds ratio; CI, 95% confidence interval

[a]Multiple logistic regression model adjusting of all relevant and significant factors in bivariate analysis

[b]'Salary' included wage and salaried employment; 'trade' included all forms of activities that created an income; 'pensions' included dependence on spouses or cash remittances

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

stable income, less education and lower CD4 cell count (Table 1). In the multivariate model, depression was associated with female gender (OR 1.62, CI 1.13–2.31, $p = 0.008$), age greater than 50 years (OR 1.93, CI 1.09–3.42, $p = 0.024$), no education compared with post-primary education (OR 1.69, CI 1.12–2.52, $p = 0.011$) and dependent income compared with trade (OR 1.81, CI 1.24–2.66, $p = 0.002$). The strongest predictor of depressive symptoms was lower CD4 cell count. Participants with a CD4 cell count between 50 and 99 were two times more likely (OR 2.0, CI 1.2–3.4 $p < 0.01$) and those with a CD4 cell count less than 50 were 2.3 times more likely (OR 2.3 CI 1.4–3.9, $p < 0.01$) to have depressive symptoms compared with participants whose CD4 cell count was >500 cells/μl (see Table 1).

Using the modified scale that excluded somatic symptoms yielded similar results. Participants with a CD4 cell count <50 cells were 2.5 times more likely (OR 2.5, CI 1.5–4.2, $p < 0.001$) to have depressive symptoms compared with participants whose CD4 cell count was >500 cells/μl. A similar response was seen with increasing CD4 cell count (data not shown).

Scale Validity

As the CES-D has not been previously validated in rural Uganda, we assessed validity in our study population by examining the factor structure of the scale items, calculating the internal consistency reliability of the sub-scales and the overall scale and examining the construct validity of the overall scale. Principal component analysis resulted in four underlying factors: depressed affect (items 3, 9, 10, 13, 14, 17 and 18), positive affect (items 4, 8, 12 and 16), somatic complaints (items 1, 2, 5, 6, 7, 11 and 20) and interpersonal concerns (items 15 and 19). All sub-scales had moderate to high internal consistency, with Cronbach's α values of 0.73 or higher (see Table 2). The overall CES-D scale was found to be internally consistent in our study population (Chronbach's $\alpha = 0.90$). The CES-D demonstrated appropriate construct validity, as women, older participants, those with no income, those with no education and those with low CD4 cell counts were more likely to report depressive symptoms (see Table 1).

Table 2 Factor structure of CES-D items among 1017 HIV infected persons in rural Uganda

Item	Content	Rotated Factor Loadings			
		Factor I *Depressed* α = 0.81	Factor II *Positive* α = 0.73	Factor III *Somatic* α = 0.79	Factor IV *Interpersonal* α = 0.87
1	Bothered by things	0.25	0.12	0.52*	0
2	Poor appetite	−0.05	0.19	0.58*	−0.24
3	Could not shake blues	0.54*	0.06	0.42	−0.16
4	As good as other people[r]	−0.05	0.51*	0.43	−0.15
5	Trouble concentrating	0.33	0.14	0.60*	−0.05
6	Depressed	0.39	0.26	0.51*	−0.25
7	Everything is an effort	0.22	0.14	0.62*	−0.12
8	Hopeful on future[r]	0.32	0.66*	−0.03	0.06
9	Life is a failure	0.68*	0.31	0.08	−0.14
10	Fearful	0.62*	0.21	0.18	−0.2
11	Trouble sleeping	0.32	0.29	0.47*	−0.1
12	Happy[r]	0.2	0.78*	0.22	−0.09
13	Like talking less	0.48*	0.08	0.36	−0.24
14	Lonely	0.44*	0.12	0.27	−0.43
15	People are unfriendly	0.1	0.07	0.09	−0.90*
16	That you enjoy life[r]	0.08	0.81*	0.14	−0.31
17	Crying	0.65*	0.09	0.13	−0.25
18	Sad	0.63*	0.23	0.29	−0.26
19	People dislike you	0.19	0.06	0.06	−0.91*
20	You could not get going	0.29	0.28	0.60*	−0.09

I. Chronbach's alpha was calculated to assess the internal consistency reliability of each sub-scales; only starred items were included in this calculation for a given factor

II. * Items loading 0.40 or greater on a given factor

[r]Items were reverse coded

Discussion

We found that the prevalence of depressive symptoms is high among HIV-infected adults living in rural Uganda and is strongly associated with lower CD4 cell count, regardless of age, education, gender or source of income. Additionally, we found the CES-D to be a valid and reliable measure of depressive symptoms in rural Uganda.

Some earlier studies from developed countries showed no association between depression and disease progression (Burack et al., 1993; Lyketsos, Hoover, & Guccione, 1996a; Lyketsos et al., 1996c), although more recent studies have documented as association (Ickovics et al., 2001; Leserman et al., 1999; Page-Shafer et al., 1996). We found a clear association between disease severity, as measured by CD4 count, and depressive symptoms. Our findings suggest that the influence of CD4 cell count on presence of depressive symptoms becomes important once the CD4 cell count falls below 100 cells/μl. This association strengthens further as the CD4 count falls below 50 cells/μl. Our findings also support previous research from industrialized countries which found that women are more likely to have depressive symptoms than men (Linn, Poku, Cain, Holzapfel, & Crawford, 1995). However, they are contrary to a study in a rural, southwestern Uganda that showed no association between depressive symptoms and gender among participants of unknown sero-status living in a high HIV prevalence area (Bolton et al., 2004). It is possible that the effect of gender is stronger among persons infected with HIV than in the general population.

While we were unable to examine a causal link in this cross-sectional analysis (Lyketsos & Treisman, 1996), persons with HIV/AIDS in Africa might benefit from interventions that offer psychosocial support. Group psychotherapy has been successfully implemented in southwestern Uganda (Bolton et al., 2003) where people have recognized depressive symptoms and considered them as consequences of the HIV epidemic (Wilk & Bolton, 2002).

Our findings suggest that the CES-D is a reliable and valid instrument for measuring depressive symptoms in rural Uganda. The scale demonstrated high internal reliability, suggesting that the 20 scale items all measured the same underlying construct, depressive symptoms. While the CES-D appears to be an accurate measure of depressive symptoms in rural Uganda, further research would be useful to establish whether depressive symptoms captured by the scale are robust in diagnosing depression and anxiety states in Africa based on the DSM-IV criteria (Breslau, 1985; Okun, Stein, Bauman, & Silver, 1996).

Our study has several potential limitations. The subjective nature of the measures used to assess depressive symptoms may have resulted in an underestimation of the prevalence of depression due to social desirability bias. Alternatively, including the somatic items in the overall CES-D scale may have led to overestimates of the prevalence of depression (Kalichman et al., 2000), as these items are common in persons with HIV. However, we found no difference in the risk factors identified or the magnitude of the associations when the analysis was re-run after removing the somatic items. In addition, our population was predominately female, so interpretations of our overall findings for gender-aggregated depression levels should take that into account. Finally, further research is needed to establish whether there is a causal relationship between depression and disease progression in Africa, whether social factors such as alcohol use and negative social experiences are associated with depression in multiple African settings, and whether there are effective interventions that could reduce depression and mitigate its effects in HIV-infected persons.

The high prevalence of depressive symptoms in this HIV-infected population in rural Africa underscores the need to include appropriate screening and treatment for depression as an important component of comprehensive care for persons with HIV.

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