PSYCHIATRIC CO-MORBIDITY IN SOUTH AFRICAN HIV/AIDS PATIENTS

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Background. To the best of our knowledge no previous studies have been published on the rates of psychopathology in HIV-infected patients from a predominantly black, heterosexual Third-World population.

Objective. To evaluate the levels of anxiety experienced by patients infected with HIV, the presence of specific anxiety and other psychiatric disorders, as well as to determine whether this is associated with disease stage and time after diagnosis.

Methods. One hundred HIV-infected patients attending the immunology clinics at the Universitas and Pelonomi hospitals in Bloemfontein, South Africa, were screened for the presence of psychiatric disorders using the Mini International Neuropsychiatric Interview (MINI). More specifically, anxiety was evaluated using the Zung self-rating and Hamilton anxiety (HAM-A) scales. Disease stage of the patient was determined by clinical examination and $CD4^+$ T-cell count values.

Results. According to the MINI, 35% of the patients had a major depressive disorder. A further 3% had dysthymic disorder, while bipolar disorder was diagnosed in 6%. As regards anxiety disorders, the following was found: panic disorder 37%, agoraphobia 9%, social phobia 15%, specific phobias 10%, obsessive-compulsive disorder 3% and generalised anxiety disorder 21%. Post-traumatic stress disorder was diagnosed in 6%. Thirty-one of the patients scored above the cut-off on both the HAM-A and Zung scales.

Conclusions. The results indicate that psychiatric co-morbidity is common in HIV-infected patients. Anxiety and depressive disorders were found in a large number of patients, significantly more than the proportion expected in the general population. The identification and treatment of these co-morbid psychiatric syndromes in HIV-infected patients should be actively pursued, as treatment could lead to an improvement in quality of life.

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HIV is carried in plasma, monocytes or lymphocytes from the peripheral blood, and enters the central nervous system (CNS) early in infection.[1,2] In fact, neurological signs and symptoms often predominate in the acute primary infection syndrome, and can include depression.[3] The pathogenesis of HIV neurological disease is unclear, but the predominant cell type infected is of monocyte-macrophage lineage, although endothelial cells, astrocytes and possibly neurons can also be infected.[4] Furthermore, once within the CNS, it is likely that infected macrophages release chemokines (such as tumour necrosis factor-α) and viral proteins (such as gp120) that may be toxic to neural cells.[5] It is, therefore, not surprising that HIV infection has been associated with several neuropsychiatric syndromes.[6]

Studies of HIV-infected patients, as well as those with AIDS, have demonstrated a negative impact of neuropsychiatric disorders on health-related quality of life and emotional well-being.[7] Generalised psychological distress, anxiety and major depressive disorders have been proposed as contributors to morbidity and even to the immune deterioration and progression of disease.[8,9] It has also been suggested that HIV infection can produce psychological effects before any physical signs of disease appear.[10,11] Differences in the psychological profiles of HIV/AIDS patients according to age, sex, race and sexual preference, as well as disease, have been recorded.[12-14]

However, all previous studies have involved HIV/AIDS patients from developed countries, with the majority being homosexual men or intravenous drug abusers. In the present study we aimed to evaluate anxiety and other psychiatric disorders in a predominantly black, heterosexual HIV/AIDS patient population from South Africa, and to determine whether these disorders are associated with disease stage, as measured by $CD4^+$ T-cell count numbers or time from diagnosis.

METHODS

One hundred HIV-infected patients attending the immunology clinics at the Universitas and Pelonomi hospitals in Bloemfontein were included in the study. The patients were known to be infected with HIV, and had been referred to the immunology clinic following the identification of anti-HIV antibodies in their serum using two enzyme-linked immunosorbent assays (Behring Enzygnost HIV-1 & 2 PLUS,

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Behringwerke and Vironostika HIV Uni-Form II, Organon Teknika). All of the patients were anti-retroviral drug-naïve at the time of study. The patients were evaluated clinically, including a full neurological and cognitive examination. The Mini Mental State Examination (MMSE) was used to evaluate cognitive function.[15] The date of diagnosis was determined for each patient from clinical records. Institutional Ethics Committee approval was obtained for the study, and after complete description of the study to the patients, written informed consent was obtained.

$CD4^+$ T-cell counts were determined by flow cytometry using a Coulter flow cytometer (EPICS Profile II) and tri-colour monoclonal antibodies (CD3 ECD, T8 FITC and T4 RD1) according to the manufacturer's instructions. The absolute $CD4^+$ T-cell count was calculated by multiplying the percentage determined on flow cytometry with the total lymphocyte count as measured using a Technicon H* 1 cell counter.

Internationally standardised psychiatric rating scales were used in this study. The three evaluators were final-year medical students trained in the use of these scales by a consultant psychiatrist. Patients were screened for specific psychiatric disorders using the Mini International Neuropsychiatric Interview (MINI).[16] More specifically, anxiety was evaluated using the Hamilton Anxiety Scale (HAM-A),[17] as well as the Zung Self-Rating Anxiety Scale.[18] The scales were administered in the language of choice of the patient, and where necessary interpreters were used. Arbitrary cut-off values of 20 and 45 were used for the HAM-A and Zung scales, respectively. The HAM-A was completed by the three evaluators simultaneously for all patients in order to control for evaluator bias. If two or more of the three observers gave a patient a HAM-A score of ≥ 20, then the patient was categorised as scoring above the cut-off.

Statistical analysis

Frequencies and percentages with 95% confidence intervals (CI) were used to describe prevalences of specific disorders. Multiple logistic regression was performed to investigate disease stage, time from diagnosis, age and sex as possible predictors of disorders as diagnosed by the MINI. Since the number of patients with certain disorders was small, *P*-values of less than 0.15 were taken to indicate a tendency, but the results should be interpreted with caution. Because of the small numbers, disease stage was categorised as group 3 ($CD4^+$ T-cell count < 200 cells/μl) versus groups 1 and 2 ($CD4^+$ T-cell count ≥ 200 cells/μl).

RESULTS

Of the 100 patients included in this study, 43% were male, and 57% female. Most of the patients were black (90%), and the predominant sexual orientation was heterosexual (94%). One patient had a history of intravenous drug abuse, and 5 had homosexual sex as a risk factor. The mean age of the patients was 32.6 years (range 17 - 64 years). The $CD4^+$ T-cell counts of the patients ranged from < 10 to 1 520 cells/μl (median = 295 cells/μl). The median time from diagnosis to inclusion in the study was 12.5 months (range 0 - 137 months). Patients were divided into three groups according to their $CD4^+$ T-cell counts, namely group 1 (> 500) ($N = 16$), group 2 (200 - 499) ($N = 57$), and group 3 (< 200) ($N = 27$). Several patients were cognitively impaired, but none presented with overt dementia. The clinical diagnoses of the patients included pneumonia, tuberculosis, chronic diarrhoea, and skin lesions. One patient, a 34-year-old man, had overt neurological impairment and presented with right hemiplegia following a cerebrovascular incident. A large percentage of the patients was physically asymptomatic, which is consistent with the fact that this was a mainly ambulant population attending an outpatient clinic, and with the fact that 73% had a $CD4^+$ T-cell count of ≥ 200 cells/μl.[3]

According to the MINI, psychiatric co-morbidity was identified in more than 50% of the patients (Table I). Thirty-one patients scored above the cut-off for both the HAM-A (≥ 20) and Zung (≥ 45) scales. Associations between specific psychiatric disorders and stage of disease, time from diagnosis, age, and sex are summarised in Table II. Major depressive disorder was associated with stage of disease; 40% of group 1 and 2 patients had a major depressive disorder, compared with 22% of group 3 patients. Stage of disease was also associated with dysthymic disorder; 7% of group 3 patients had the disorder, compared with only 1% of group 1 and 2 patients. Dysthymic disorder, bipolar disorder, agoraphobia and social phobia were associated with time from diagnosis, with patients who had been diagnosed for a longer time being at increased risk. Younger patients were more likely to have bipolar disorder, and older patients to have generalised anxiety disorder. Female patients were more likely to have panic disorder (46% of females, compared with 26% of males), and

Table I. Prevalences of psychiatric syndromes in HIV/AIDS patients

	Number of patients ($N = 100$)	95% CI
Total co-morbidity	58	47.7; 67.8
Major depressive disorder	35	25.7; 45.2
Dysthymic disorder	3	0.6; 8.5
Bipolar disorder	6	2.2; 12.6
Panic disorder	37	27.6; 47.2
Agoraphobia	9	4.2; 16.4
Social phobia	15	8.7; 23.5
Specific phobia	10	4.9; 17.6
Obsessive-compulsive disorder	3	0.6; 8.5
Generalised anxiety disorder	21	13.5; 30.3
Post-traumatic stress disorder	6	2.2; 12.6
Substance abuse	7	2.9; 13.9

Table II. Associations between specific psychiatric disorders and stage of disease, time from diagnosis, age, and sex — odds ratios from multiple logistic regression

	Stage of disease (group 3 v. groups 1/2)	Time from diagnosis (months)	Age (years)	Sex (M/F)
Major depressive disorder	0.428*	1.007	1.007	0.839
Dysthymic disorder	30.433*	1.079*	1.022	0.086
Bipolar disorder	0.769	1.039*	0.832*	1.629
Panic disorder	0.533	1.010	0.979	0.426*
Agoraphobia	1.609	1.023*	0.954	1.768
Social phobia	0.950	1.017*	1.021	0.779
Specific phobia	2.007	1.000	0.980	1.395
Obsessive-compulsive disorder	-†	-	-	-
Generalised anxiety disorder	0.652	0.999	1.082*	0.637
Post-traumatic stress disorder	0.556	0.993	0.988	0.684
Substance abuse	1.866	0.987	1.012	8.470*

* $P < 0.15$.
† This was not calculated as the model fit was questionable.

males were more likely to be substance abusers (14% of males compared with 2% of females).

Discussion

To the best of our knowledge, this is the first study on the prevalence of psychiatric comorbidity in a population of mainly black, heterosexual HIV/AIDS patients from a developing country. The main objective was to determine the rates of psychopathology in an otherwise psychiatrically underserved subgroup of the population. In South Africa the majority of HIV/AIDS patients are to be found in the heterosexual black population. Many of these patients will at some stage of their disease be treated by traditional healers,[19] often using substances that may have psychotropic effects. The information obtained from a study on psychiatric co-morbidity in predominantly black HIV/AIDS patients could provide valuable data regarding the psychiatric treatment requirements of these individuals.

The results from the present study clearly demonstrate that psychiatric co-morbidity is common in South African HIV/AIDS patients. Anxiety and depressive disorders were found in a large number of patients. Unfortunately, the interpretation of these results is complicated by the fact that prevalences for the various psychiatric syndromes in the general South African population are not known. Further studies of psychiatric co-morbidity in this population should, therefore, include a control group of HIV-seronegative people. However there has been one study done on the prevalence of major depressive disorder in a black rural population in South Africa. This study demonstrated a prevalence of 18.9%,[20] which is significantly lower than the 35% recorded in the HIV/AIDS patients included in the present study. A limitation of the study by Jordaan *et al.*[20] is the fact that patients were not screened for the presence of adjustment disorders. Screening for this should be included in future studies.

The validity of these psychiatric rating scales, which were initially developed for the screening of predominantly Caucasian populations from developed countries, should also be scrutinised and standardised for the population in this country. In order to overcome this problem to a certain extent, scales were translated and interpreters used to make the scales as culturally friendly as possible. However further research needs to be undertaken in this regard.

Most of the associations with age and sex given in Table II are consistent with what would be expected in a psychiatric sample. Of interest is the fact that the prevalence of major depressive disorder was significantly higher in patients with earlier stage disease (groups 1 and 2), than in patients with more advanced immunosuppression (group 3). An explanation for this is not immediately at hand. Inhibition of neuroleukins might play a role in the neuropsychiatric sequelae of HIV,[21] and if such an inhibition is immune-mediated, it would be expected to decrease with progressive immune system degeneration and progression of disease. However, it is clear that further studies on the neurophysiological correlates of psychopathology in HIV/AIDS patients are needed.

Diffuse cognitive deficits were identified in several patients, but none presented with overt dementia. This finding does not fit in with what is to be expected in the HIV/AIDS population in general, as it is estimated that approximately 25% of HIV-infected patients will eventually develop dementia.[22] The most likely explanation for the absence of dementia seen in this study is the fact that patients were recruited from a mainly ambulatory outpatient population. Patients with severe cognitive dysfunction were unlikely to have been able to attend the clinic and be considered for inclusion in the study. Moreover, the risk for AIDS dementia increases as immunological function decreases, and as the majority of patients (73%) had a $CD4^+$ T-cell count of ≥ 200 cells/μl, a high rate of cognitive impairment would not have been expected in this population. Furthermore, the MMSE has in the past failed to identify consistently all patients with dementia,[23] and the possibility of its seriously underestimating the rate of cognitive impairment in this population should be considered. It might be inappropriate to rely solely on this instrument to recognise HIV/AIDS patients with cognitive deficits,[24] and more sensitive screening tools should be employed in this setting.

In summary, psychiatric co-morbidity was extremely prevalent in this predominantly heterosexual, black HIV/AIDS population. The psychological impact of the diagnosis of HIV/AIDS is unlikely to be the only and determining cause of

the development of psychopathology in these patients, but the role of this stress factor cannot be excluded. The correct diagnosis and treatment of co-morbid psychiatric disorders is clearly important. Quality of life and progression of disease may be directly linked to this and it is, therefore, of paramount importance in the care and management of HIV / AIDS patients. A routine consultation-liaison with psychiatric services is recommended and is, in our opinion, of crucial value.

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References

1. Gabuzda DH, Hirsch MS. Neurologic manifestations of infection with human immunodeficiency virus — clinical features and pathogenesis. *Ann Intern Med* 1987; **107:** 383-391.
2. Price RW, Brew B, Sidtis J, Rosenblum M, Scheck AC, Cleary P. The brain in AIDS: central nervous system HIV-1 infection and the AIDS dementia complex. *Science* 1988; **239:** 586-589.
3. Ho DD, Sarngadharan MG, Resnick L, Dimarzo-Veronese F, Rota TR, Hirsch MS. Primary human T-lymphotropic virus type III infection. *Ann Intern Med* 1985; **103:** 880-883.
4. Wiley CA, Schrier RD, Nelson JA, Lampert PW, Oldstone MBA. Cellular localization of human immunodeficiency virus infection within the brains of acquired immunodeficiency syndrome patients. *Proc Natl Acad Sci USA* 1986; **83:** 7089-7093.
5. Hirsch MS, Curran J. Human immunodeficiency virus. In: Fields BN, Knipe DM, Howley PM, *et al.*, eds. *Fields Virology.* Philadelphia, PA: Lippincott-Raven Publishers, 1996.
6. Forstein M. The neuropsychiatric aspects of HIV infection. *Prim Care* 1992; **19:** 97-117.
7. Sathiamoorthy K, Suniti S, Kumarasamy A, Ganesh K. Neuropsychiatric morbidity in early symptomatic HIV infection. XIth International Conference on AIDS. Vancouver, 5-12 July 1996.
8. Krikorian R, Kay J, Liang WM. Emotional distress, coping, and adjustment in human immunodeficiency virus infection and acquired immunodeficiency syndrome. *J Nerv Ment Dis* 1995; **183:** 293-298.
9. Perretta P, Nisita C, Zaccagnini E, *et al.* Psychopathology in 90 consecutive immunodeficiency virus-seropositive and acquired immune deficiency syndrome patients with mostly intravenous drug use history. *Compr Psychiatry* 1996; **37:** 267-272.
10. Perry S, Jacobsberg LB, Fishman B, Frances A, Bobo J, Jacobsberg BJ. Psychiatric diagnosis before serological testing for the human immunodeficiency virus. *Am J Psychiatry* 1990; **147:** 89-93.
11. Jones QJ, Garsia RJ, Wu RT, Job RF, Dunn SM. A controlled study of anxiety and morbid cognitions at initial screening for human immunodeficiency virus (HIV) in a cohort of people with haemophilia. *J Psychosom Res* 1995; **39:** 597-608.
12. Cole SW, Kemeny ME, Taylor SE, Visscher BR, Fahey JL. Accelerated course of human immunodeficiency virus in gay men who conceal their homosexual identity. *Psychosom Med* 1996; **58:** 219-231.
13. Linn JG, Poku KA, Cain VA, Holzapfel KM, Crawford DF. Psychosocial outcomes of HIV illness in male and female African American clients. *Soc Work Health Care* 1995; **21:** 43-60.
14. Weinrich JD, Atkinson JH, McCutchan JA, Grant I. Is gender dysporia dysphoric? Elevated depression and anxiety in gender dysphoric and non-dysphoric homosexual and bisexual men in an HIV sample. HNRC group. *Arch Sex Behav* 1995; **24:** 55-72.
15. Tangalos EG, Smith GE, Ivnik RJ, *et al.* The Mini Mental State Examination in general medical practice: clinical utility and acceptance. *Mayo Clin Proc* 1996; **71:** 829-837.
16. Lecubrier Y, Sheehan DV, Weiller E, *et al.* The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: Reliability and validity according to the CIDI. *European Psychiatry* 1997; **12:** 224-231.
17. Hamilton M. The assessment of anxiety states by rating. *Brit J Med Psychol* 1959; **22:** 50-54.
18. Zung WK. A rating instrument for anxiety disorders. *Psychosomatics* 1971; **12:** 371-379.
19. Sher R. First and third world bioethics in South Africa. *Modern Medicine* 1994; **8:** 72-77.
20. Jordaan HL, Gagiano CA, Joubert G. Prevalence of depression among black patients in a primary care practice. *Geneeskunde* 1994; **8:** 27-34.
21. Fauci AS. The human immunodeficiency virus: infectivity and mechanisms of pathogenesis. *Science* 1988; **239:** 617-622.
22. Fauci AS, Lane HC. Human immunodeficiency virus (HIV) disease: AIDS and related disorders. In: Fauci AS, Braunwald E, Isselbacher KJ, *et al.*, eds. *Harrison's Principles of Internal Medicine,* Vol 2. New York: McGraw-Hill, 1998.
23. Folstein MF, Fetting JH, Lobo A, Niaz U, Capozzoli KD. Cognitive assessment of cancer patients. *Cancer* 1984; **53**(S10): 2250-2257.
24. Faustman WO, Moses JA, Csernansky JG. Limitations of the Mini Mental State Examination in predicting neuropsychological functioning in a psychiatric sample. *Acta Psychiatr Scand* 1990; **81:** 126-131.

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