Effect of Progression of Disease on Cognitive Performance in HIV/AIDS

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Background: HIV infection causes a range of cognitive and behavioral symptoms that become more frequent and severe as the immune system deteriorates and symptomatic illness ensues.

Objective: To determine the impact of disease progression on cognitive abilities of Nigerian Africans who present in the HIV/AIDS clinic of the University Teaching Hospital, Benin City, Nigeria, using the CD_4 levels as the measure of disease progression.

Methods: A total of 288 subjects comprising 96 randomly selected symptomatic AIDS patients, 96 randomly selected asymptomatic HIV-positive patients and 96 HIV-negative controls participated in the study. Enzyme-linked immunosorbent assay (ELISA) method was used to detect HIV infection, and CD_4 levels were obtained for all subjects. The Community Screening Interview for Dementia (CSI 'D') was used to assess cognitive performance of subjects. Subjects were matched for age, sex and level of education.

Results: Each category of subjects comprised 48 males and 48 females. The mean ages were 32.94 ± 8.0 years, 31.47 ± 6.7 years and 33.56 ± 7.1 years for the controls, asymptomatic HIV-positive and symptomatic AIDS subjects respectively (p=0.127). The mean CD_4 levels were 684 ± 44/μL (controls), 284 ± 62/μL (asymptomatic HIV positive) and 142 ± 36/μL (symptomatic AIDS). The mean CS1 'D' scores were 66.46 ± 1.90 (controls), 66.31 ± 2.14 (asymptomatic HIV positive) and 56.62 ± 4.23 (symptomatic AIDS).

Conclusion: Cognitive abilities of HIV/AIDS patients decline as the disease progresses. This is reflected in the cognitive performances of the symptomatic AIDS patients. The lower the CD_4 levels, the worse the cognitive deficits. There was, however, no significant difference in the performance of asymptomatic HIV-positive patients and the controls.

Key words: HIV/AIDS ■ cognition ■ CD_4 levels

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INTRODUCTION

The nervous system is affected not only by opportunistic infections but also directly or indirectly by HIV itself. Consequently, neurological complications have been described in patients with AIDS, and these constitute the initial manifestations in 7–20% of patients with asymptomatic HIV infection.[1-3] This prevalence increases to 39–70% in symptomatic HIV infection.[1,4,5]

The most dramatic impact of HIV on the central nervous system (CNS) is seen in the form of cognitive/motor impairments.[6,7] Initially, it was believed that these impairments were secondary to opportunistic infections, CNS tumors and other medical conditions associated with advancing HIV disease, but there are reports of cognitive dysfunctions in asymptomatic HIV-positive persons.[1,7]

Cognitive disturbances, in turn, result in everyday functional impairment. Subclinical deficits in test performances are frequent and detectable in the asymptomatic stages of the illness.[3,4,7] With the increasing incidence of HIV/AIDS in sub-Saharan Africa, where the disease is responsible for >2 million deaths[8,9] and 15,000 new cases annually,[10] cognitive impairments associated with HIV will significantly affect quality of life and increase mortality. There is no data on the cognitive performance of Nigerian Africans with HIV/AIDS, thus making this study unique. We assessed the cognitive performances of both the asymptomatic HIV-positive and symptomatic AIDS patients and compared their performances with HIV-negative controls using the CD_4 levels as the measure of disease progression.

PATIENTS AND METHODS

A total of 192 patients with positive enzyme-linked immunosorbent assay (ELISA) test results for HIV infection were randomly recruited from the HIV/AIDS clinic of the University Teaching Hospital, Benin City, Nigeria, using a table of random numbers, over a six-month period (January to June 2004). These patients consisted of 96 HIV-seropositive asymptomatic and 96 symptomatic AIDS subjects. Ninety-six seronegative volunteers were selected randomly from the outpatient

department, antenatal clinics and among hospital staff members. The three groups of subjects were matched for age, sex and level of education. Informed consents were obtained from the subjects and controls, and approval to undertake the study was granted by the Hospital Ethics Committee.

Demographic variables were obtained from the subjects using a questionnaire by one of the authors (Odiase). The inclusion criteria included HIV seropositivity—asymptomatic individuals >18 years of age and symptomatic AIDS patients >18 years of age. Subjects who were <18 years of age, already on antiretroviral therapy, with comorbidities [diabetes mellitus, hypertension epilepsy and associated intracranial disorders (for example, brain tumor) and other metabolic diseases], with inconclusive diagnosis, major axis-1 psychiatric illness, with presence of clinical signs of cardiac failure, alcohol intake >120 g/week or 13 units/week, history of previous head injury with loss of consciousness and on anticholinergic medications were excluded from the study.

The cognitive testing was done with a 33-point instrument—Community Screening Instrument for Dementia (CSI 'D').[11] This test instrument has been widely used among Nigerians in the Ibadan-Indianapolis Dementia project[12] and has been validated in our center.[13] Full clinical examination, CD_4 counts, liver function tests, electrolytes, erythrocyte sedimentation rate and complete blood count were carried out for all subjects. Neuroimaging [computerized tomographic (CT) scan of the brain] was done where indicated.

Statistical analysis of data was done with the aid of EpiInfo™ 2000 software. Means of subjects' ages, CD_4 levels and cognitive performances were compared for statistical significance using two-way analysis of variance (ANOVA) test. The level of significance was taken as $p<0.05$.

RESULTS

The mean ages were 32.94 ± 8.0 years, 31.47 ± 6.7 years and 33.56 ± 7.1 years, respectively, for the controls, asymptomatic HIV-positive patients and those with symptomatic AIDS. There was no statistically significant difference in the means of their ages ($p>0.05$). Mean CD_4 levels for the controls, asymptomatic HIV-positive and symptomatic AIDS patients were 684 ± 44/μl, 285 ± 62/μl and 142 ± 36/μl, respectively ($p<0.01$). The average CSI 'D' scores were 66.46 ± 1.79 (controls) 66.31 ± 2.14 (asymptomatic HIV-positive patients) and 56.62 ± 4.23 (symptomatic AIDS patients). The mean CSI 'D' score of the controls was not significantly different from that of the asymptomatic HIV-positive patients ($p=0.13$), but was significantly different from the mean score of patients with symptomatic disease ($p<0.01$). Abnormal CSI 'D' scores were recorded in 32.6% of asymptomatic HIV-positive individuals compared to 99% of patients with symptomatic illness ($p<0.01$).

DISCUSSION

Several studies have reported cognitive impairments among asymptomatic HIV-positive patients and those with established AIDS[14-16] and are usually characterized by subtle psychomotor and mental slowing initially, but affecting other cognitive domains as the disease progresses.[15] These cognitive impairments have also been linked with disturbances in various activities of daily living,[17] poor adherence to HAART[18] and with reduced ability to work.[19]

Neuropathologically, HIV is a neurotropic virus, entering the CNS primarily via infected blood mononuclear cells (macrophages). HIV does not necessarily produce its disturbances by directly infecting neuronal cells but more likely by the toxic effects of HIV envelope proteins such as gp 120, and by various neurotoxic by-products [e.g., tumor necrosis factor (TNF)-alpha, quinolinic acid] that result from macrophages, and astrocytes proliferation and activation driven by HIV replication in CNS.[20,21] These mechanisms may result in neuronal dysfunction and apoptosis which then produce cognitive, motor and behavioral disturbances. Hence, subcortical brain structures are the regions primarily affected.

Our study did not show any statistically significant difference in cognitive performances of controls and asymptomatic HIV-positive patients, though one-third of the latter group had abnormal cognitive results. This observation has been reported by some other authors.[22-24] It is possible that the cognitive dysfunction in the asymptomatic stage of HIV infection is subtle requiring more sensitive neurocognitive test batteries for its detection or that the different cognitive tests reported in the literature measure different cognitive domains, making interpretation and standardization of results difficult. It is also possible that asymptomatic HIV patients do not have cognitive dysfunctions. This last possibility is, however, the least likely to be correct because there have been reports of mild (subsyndromic) cognitive abnormalities in neuropsychological testing of persons with asymptomatic infection.[25] A specific link to HIV as the sole cause of these mild abnormalities was often difficult to establish. That the introduction of HAART has resulted in significant reduction in the prevalence of cognitive impairments in HIV infection strongly suggests the involvement of the virus in the genesis of neurocognitive dysfunction.[26,27]

Our study corroborated earlier reports[18,19] of occurrence of cognitive impairments specifically related to HIV infection during advanced stages of the disease and in the setting of severe immunosuppression. A prevalence of 12–87% of cognitive symptoms was reported among patients with established disease.[28] Studies have also shown that at least one-third of persons with symptomatic HIV infection have at least mild neuropsychological impairment.[29-31]

CONCLUSION

This study has confirmed the presence of neurocognitive impairments in patients with symptomatic HIV infection, and significant decline in cognitive performance with progression of HIV disease. Depending on the severity, neurocognitive impairments may affect the quality of life of patients with HIV/AIDS. Recognizing this fact prompts the use of early, appropriate HAART and, possibly, additional treatment to help patients compensate for deficits in functioning. Neuropsychological assessment should be mandatory for all HIV-positive patients.

ACKNOWLEDGEMENT

The Dementia Project Unit of the University College Hospital for the permission to use the CSI 'D' instrument.

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