The International HIV Dementia Scale Is a Useful Screening Tool for HIV-Associated Dementia/Cognitive Impairment in HIV-Infected Adults in Yaoundé—Cameroon

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Objective: As a baseline for a series of studies on HIV-associated dementia (HAD), we sought to assess the usefulness of the recently developed International HIV Dementia Scale (IHDS) as a screening tool for HAD or HIV-associated cognitive impairment (HACI) in HIV-positive adults in Yaoundé—Cameroon.

Design: The frequency of HAD/HACI is largely unknown in resource-limited countries. In Cameroon, few studies suggest that HAD may be frequent but no specific study had so far investigated the problem. We therefore used a case–control study design involving HIV-positive adults as cases and HIV-negative individuals as controls to determine the usefulness of the IHDS as a screening instrument.

Methods: HIV-positive adults followed up in an HIV outpatient clinic were matched to HIV-negative subjects for age and sex and screened using IHDS.

Results: Overall, 204 HIV-positive individuals and 204 HIV-negative subjects were screened. The HIV-positive subjects had a significantly lower IHDS mean total score of 10.87 compared with the HIV-negative subjects with a score of 11.28 ($P = 0.00$). Abnormal scores (≤ 10) on the IHDS were found in 21.1% of the HIV-positive subjects and in 2.5% of the HIV-negative subjects ($P = 5.0 \times 10^{-10}$).

Conclusions: These results suggest that the prevalence of possible HAD/HACI may be higher in Cameroon than the previous estimates and demonstrate that the IHDS can be used as a screening tool for HAD in Cameroon. We therefore suggest that all studies on HAD in Cameroon should strategically start with the IHDS as a screening tool.

Key Words: HIV/AIDS, cognitive impairment, dementia, IHDS, Cameroon, Sub-Saharan Africa

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The authors have no conflict of interest to declare.

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INTRODUCTION

HIV-associated dementia (HAD) is an important neurological complication of advanced HIV infection. It is the first most encountered encephalopathic complication in Europe, affecting cognitive and motor abilities.[1] The frequency of this disorder is largely unknown in resource-limited countries although preliminary surveys in Uganda[2] and India[3] suggest a relatively high frequency of cognitive dysfunction. In Cameroon, our group found that 6.60% of the studied 108 patients with HIV had the AIDS-Dementia Complex (ADC).[4] Our previous work on the scanographic and clinical aspects of cerebral lesions in HIV-infected patients showed that 14.9% of the subjects had diffuse cerebral atrophy attributed to HIV encephalitis.[5] This suggests that HAD may be frequent in Cameroon. Because no specific study has been carried out in Cameroon on HAD or HIV-associated cognitive impairment (HACI), we planned a series of studies on this complication of HIV AIDS. The first of these studies, that we report here, was aimed at assessing the usefulness of the simple, recently developed International HIV Dementia Scale (IHDS) as a screening tool for HACI/HAD.

With the advent of highly active antiretroviral therapy, the incidence of HAD has been decreasing in the United States,[6] but with continued survival, the prevalence of this disorder has actually increased.[7] Given the increased prevalence of HAD and its negative impact on quality of life,[8] the morbidity of HAD is potentially significant especially in developing countries like Cameroon where large numbers of people are infected with HIV. HAD is associated with an increased risk of mortality[9,10]; it can affect antiretroviral therapy adherence, which is essential for suppression of viral replication,[11] and it is a potentially treatable condition with highly active antiretroviral therapy.[12,13]

HAD is a subcortical dementia characterized by cognitive, behavioral, and motor dysfunction. Typically, there is memory impairment, the inability to manipulate acquired knowledge, apathetic personality changes, and generalized slowing of thought processes.[14] HACI constitutes the milder end of a continuum of the disease that moves from mild deficit through severe dementia. It describes difficulties with thinking, problem solving, and concentration in addition to memory impairment that is not severe enough to fulfill the *DSM-IV* criteria for dementia.

The diagnosis of either HAD/HACI requires subjecting suspected individuals to a battery of neuropsychological

tests that usually require specialized personnel, and the administration is very time consuming. Therefore, there is a great need in resource-limited countries to have a simple screening test to identify subjects who are most at risk and who would then undergo the complete battery of neuropsychological testing for confirmation of diagnosis and subsequent management.

OBJECTIVES

The specific objectives of this baseline study were (1) to screen a group of HIV-positive patients and HIV-negative subjects in Yaoundé using the IHDS, (2) to determine the prevalence of HACI and the value of the IHDS as a screening tool in our context, and (3) to propose a strategy for future studies on HAD in Cameroon.

METHODS

Study Setting

The Day Care Hospital is the first of several HIV follow-up and treatment centers in the country created by the Ministry of Public Health through the National Aids Control Committee. It is a well-recognized treatment center in which about 16,000 HIV-positive patients are followed up, of whom 3000 are on antiretroviral therapy as of 2006. It receives a variety of patients from all over the country.

Study Design

We used a case–control study design involving HIV-positive adults as cases and HIV-negative individuals as controls to determine the usefulness of the IHDS as a screening instrument.

Patients and Data Collection

The HIV-positive patients were recruited consecutively in the Day Care Hospital, which is the HIV outpatient clinic of the Yaoundé Central Hospital, in Yaoundé, the capital of Cameroon, from September 2006 to December 2006. The control HIV-negative subjects were recruited in the HIV voluntary counseling and testing sections of the Day Care Hospital, the central maternity, both of the Yaoundé Central Hospital, and the Health and Social Welfare Centre of the University of Yaoundé I. HIV-positive patients were matched for age and sex with the HIV-negative subjects during the same study period.

Well-documented HIV-positive patients aged 18–60 years who gave a written consent to participate in the study (cases) were included irrespective of whether they were on treatment or not and irrespective of the CD4 count. Confirmed HIV-negative adults, aged 18–60 years, with HIV test results at most 6 months old and who gave written consent to the study were included as controls and matched with the cases for sex and age. Exclusion criteria were (1) present or past history of diffuse or focal central nervous system (CNS) disease, (2) head trauma, (3) current systemic disease, (4) alcohol abuse (CAGE questionnaire), (5) known psychiatric disease or treatment with antipsychotic drugs, and (6) fever of 37.5°C.

In addition to the administration of the IHDS, each patient and control subject underwent a complete medical history and physical examination including a thorough neurological assessment at the outpatient consultation clinic. Interviews were in French, English, or Pidgin English depending on the language best-mastered by the subject. Additional information was obtained from the patients' case files. Handedness was determined using the BRYDEN index in situations of ambiguity.[15] Screening for HAD/HACI was done using the IHDS cutoff value of ≤ 10.[16] All data were recorded in predesigned questionnaires. Data analysis was done with Epi Info 2006 (version 3.3.2) statistics and data software of the Centers for Disease Control and Prevention (CDC) for public health analysis. For all tests, a P value of <0.05 was considered significant. Mean and SDs were computed for the IHDS composite score and each of its components for each of the groups. Comparisons between the groups were made by analysis of variance. χ^2 test was used where appropriate.

Ethical clearance was obtained from the National Ethics Committee, and an administrative authorization for research was delivered for this study by the Minister of Public Health.

The IHDS and Adaptation

The IHDS is a modification of the HIV dementia scale first proposed by Power et al (1995) and recently adapted by Sacktor et al[16] (2005). This tool is important in that it is (1) easy to administer; (2) easy to train health professionals, not necessarily neurologists; (3) less costly, needing no sophisticated instrumentation other than a watch with a second hand; and (4) independent of language and culture. This tool if validated could be used to identify patients at risk for HAD without the need for extensive, very long, and costly neuropsychological tests that are even almost inexistent in Cameroon.

The IHDS consists of 3 subsets: timed fingertapping which measures motor speed; timed alternating hand sequence which assesses the psychomotor speed; and recall of 4 items at 2 minutes which assesses memory registration and recall. Each of these subtests is rated on a scale of 0–4. The tests were administered as follows: for assessment of the verbal recall subtest, registration (new learning) was measured by reciting 4 words to the subject (*red*, *dog*, *hat*, and *bean*) taking 1 second to say each of the words. We did an adaptation with the translation of these words in French thus: *chien*, *camion*, *rouge*, *enseignant*. The subject was asked to repeat the words. If the subject did not repeat all the words immediately, the examiner repeated all the words until the subject could repeat all the 4 words correctly. He/she was then asked to recall the 4 words after the timed fingertapping, and alternating hand sequence tests were performed. For words not recalled, the subject was prompted with a semantic clue as follows: animal (dog), piece of clothing (hat), vegetable (bean), and color (red) or the French equivalent of the words: *animal (chien)*, *véhicule (camion)*, *couleur (rouge)*, and *profession (enseignant)*. One point was given for each word recalled spontaneously and 0.5 points for each word recalled after prompting.

For the assessment of motor speed, the number of fingertaps of the first 2 fingers of the nondominant hand was measured by instructing the participant to open and close the fingers as widely and as quickly as possible over a 5-second period. Points were assigned as follows: 4 = ≥15 taps/5 s;

3 = 11–14 taps/5 s; 2 = 7–10 taps/5 s; 1 = 3–6 taps/5 s; and 0 = 0–2 taps/5 s. In the alternating hand sequence for assessing the psychomotor speed, the subject was asked to perform the following movement in succession with the nondominant hand as quickly as possible over a 10-second period: (1) clench the hand in a fist on a flat surface, (2) put the hand flat on the surface with the palm down, and (3) put the hand perpendicular to the flat surface on the side of the fifth digit. The 3 hand positions were demonstrated to the participant by the examiner, and the participant would then perform the sequence correctly twice for practice before the 10-second subtest was performed. The task was scored as follows: 4 = 4 sequences in 10 seconds; 3 = 3 sequences in 10 seconds; 2 = 2 sequences in 10 seconds; 1 = 1 sequence in 10 seconds; and 0 = 0 sequence in 10 seconds. Timing was done using a 1/100th second stopwatch (Professional Quartz Timer). The total score out of 12 was calculated for each participant, with each of the 3 subtests contributing 4 points maximum to the total score. For our study, an IHDS score of ≤10 was considered abnormal.

The sensitivity and specificity for the detection of HAD/HACI for an IHDS score of ≤10 have been shown to be 80% and 55%, respectively, in a Ugandan cohort and 80% and 57% in a US cohort.[16]

RESULTS

Two hundred four HIV-positive patients (cases) were included and matched for age and gender to 204 HIV-negative subjects (controls). Two cases with hemiparesis and 3 with Bell palsy were excluded from the study. The sociodemographic characteristics of the subjects are shown in Table 1. There were no age or sex differences between the HIV-positive and HIV-negative subjects. The mean age of the HIV-positive patients was 37.2 ± 8.8 years (mean ± SD), with range 18–59 years, whereas that of the HIV-negative subjects was 37.1 ± 8.7 years (range 18–58 years), $P = 0.9100$. Females made up 68.6% of both the cases and the controls. The mean age of females was 35.85 ± 8.4 years and that of the males was 40.26 ± 8.85 years, $P = 0.0006$. The number of years of education for HIV-positive subjects was 11.12 years, whereas that of the HIV-negative subjects was 12.96 years, $P = 0.9141$. Within the group of HIV patients, there was no significant difference between the patients with IHDS ≤10 (cognitive impairment) and those with IHDS >10 (no cognitive impairment) with respect to the level of education, $P = 0.57$. The mean CD4 count of the patients was 265 ± 194 cells/μL (n = 185). Seventy-five (40.5%) had CD4 counts <200/μL.

The HIV-positive subjects had a mean IHDS score of 10.87 ± 0.91, whereas the HIV-negative subjects scored 11.28 ± 0.56 ($P < 0.00001$). The number of HIV patients with IHDS total score ≤10 (abnormal) was 43 (21.1%), whereas just 5 HIV-negative subjects (2.5%) had an IHDS score of ≤10, $P = 5.0 \times 10^{-10}$.

The prevalence of possible HACI in this study defined by an IHDS score of ≤10 was therefore 21.1% with 95% confidence interval of 15.7% to 27.3%. The mean total IHDS score of HIV patients with abnormal scores was 9.49 ± 0.68, whereas HIV-negative subjects scored 11.25 ± 0.53 ($P < 0.00001$). For the HIV-negative subjects with abnormal scores, the mean IHDS score was 9.90 ± 0.22, whereas those with normal scores had a mean IHDS score of 11.31 ± 0.51, $P < 0.00001$. Table 2 shows the comparison between the 2 groups with respect to the mean IHDS scores on the 3 components of the test. In the psychomotor speed subtest, there was a significant difference between the HIV-positive and HIV-negative groups, $P = 0.0051$. Twenty-two HIV-positive subjects (10.8%) scored ≤ 3, whereas just 8 HIV-negative subjects (3.9%) scored ≤ 3. In the memory recall subtest, there were significant differences between the 2 groups as well, $P < 0.00001$. Eighteen (8.8%) HIV-negative subjects scored ≤ 3, whereas 51 (25%) HIV-positive subjects scored ≤ 3. Whereas 91.2% of the HIV-negative subjects had a score ≥ 3.5, 75% of the HIV-positive subjects had a score ≥ 3.5. There was no difference in the motor speed subtest between the 2 groups, $P = 0.1797$.

In the HIV-positive group, 25 of the 75 patients (33.3%) with CD4 counts <200/μL (CDC class III) had an IHDS score ≤10, whereas 16 of the 110 patients (14.5%) with CD4 counts 200–499/μL (CDC class II) had a score ≤10, and only 8% of CDC class I patients (CD4 counts ≥500/μL) had an abnormal score ($P = 0.003$). The mean IHDS score of patients with CD4 ≥200/μL was 11.0545 ± 0.8442 whereas that of patients with CD4 <200/μL was 10.5933 ± 0.9540 ($P = 0.0007$). The proportion of cases with abnormal IHDS for patients with CD4 ≥200/μL was 39.0% (16/41), confidence limits: 24.2%–55.5% whereas that of patients with CD4 <200/μL was 61.0% (25/41), confidence limits: 44.5%–75.8%.

TABLE 1. Sociodemographic and Clinical Characteristics of the Study Subjects

Variable	HIV Negative (n = 204)	HIV Positive (n = 204)	*P* value
Sex, No. (%)			
Male	64 (31.4)	64 (31.4)	0.003
Female	140 (68.6)	140 (68.6)	0.003
Mean age (yr)	37.1 ± 8.7	37.2 ± 8.8	0.9100
Male	40.2 ± 8.9	40.3 ± 8.9	0.961
Female	35.9 ± 8.3	35.8 ± 8.4	0.962
Education (yr)	12.96	11.12	0.9141
Mean CD4 counts/μL	NA	265 ± 194	NA

NA, not available.

TABLE 2. Comparison of the IHDS Scores Between the HIV-Positive and HIV-Negative Subjects

	HIV-Negative Group	HIV-Positive Group	
	Controls (n = 204)	Cases (n = 204)	*P* value
IHDS total score	11.28 (0.56)	10.87 (0.91)	0.0000
IHDS fingertapping subscore	3.4 (0.5)	3.4 (0.5)	0.1797
IHDS alternating hand sequence	3.96 (0.20)	3.88 (0.34)	0.005
IHDS 4-word recall	3.9 (0.3)	3.6 (0.6)	<0.00001

Values are given as mean values (± SD).

DISCUSSION

This is the first study in Cameroon and Central Africa that has evaluated the usefulness of the IHDS in patients with AIDS. In our study, the IHDS was successfully used to screen for cases of HAD/HACI. The mean total IHDS score of the HIV-positive subjects was significantly lower than that of HIV-negative subjects ($P < 0.00001$). The mean total score in our controls is very similar to that obtained in the Ugandan counterparts.[16] On the contrary, the mean total score of 10.87 ± 0.91 for cases (as against 11.23 ± 0.56 in controls) is higher than the figure reported in the study in Uganda where the mean value in HIV-positive subjects was 9.9 ± 3.6 as against 11.0 ± 1.0 in HIV-negative subjects ($P < 0.0000001$).[16] It is unlikely that this difference is due to age as suggested in the Ugandan cohort, given that both our cases and controls were older than the Ugandan counterparts. We suspect that differences in disease stage in the 2 samples may explain this situation.

Considering the subtests of the IHDS, our data showed that the differences between the HIV-positive and HIV-negative subjects were statistically significant for both the memory recall ($P < 0.00001$) and the psychomotor speed ($P = 0.004$). These findings are similar to those obtained in 2 earlier studies in the United States and Uganda (2005) and in India (2006), where it was found that these portions of the IHDS were the most sensitive in picking up the early changes associated with HAD.[3,16] On the other hand, there was no significant difference in the mean IHDS fingertapping subscore (motor speed), $P = 0.1797$, similar to findings in the Indian study, unlike the finding in the Ugandan study. The difference in the motor speed in the former study was attributed to the fact that the HIV-positive cohort was significantly older than the HIV-negative cohort, and age is associated with motor performance decline, especially in the fifth and sixth decades of life. Because cases and controls were matched for age in the current study, the influence of the age factor was excluded. This may suggest that the value of the fingertapping subtest is probably limited compared with the total score, the psychomotor speed, and the memory recall. This observation requires further study.

We further observed that performance on the IHDS testing did indicate neurological disease severity as the proportion of patients with HIV with an abnormal IHDS score (≤ 10) increased from CDC class I to class III patients. We recognize that this is not a perfect correlation for individual patients but remains true for group studies.

The prevalence of possible HACI in this study was 21.1% with 95% confidence interval of 15.7% to 27.3%. This was significantly different from the percentage of cognitive impairment in HIV-negative subjects, $P = 5.0 \times 10^{-10}$, odds ratio (OR) = 10.6. It is also higher than the frequency of AIDS–dementia complex and HIV encephalitis found in earlier Cameroonian studies.[4,5] This suggests that the prevalence of HAD/HACI may be highly underestimated in Cameroon. Unlike the study in India where up to 15% of the HIV-negative subjects had abnormal scores, only 2.5% of our HIV-negative subjects had abnormal scores. However, we considered as normal all subjects with IHDS score >10, whereas the Indian study used ≥ 10 as normal. This may explain the observed differences. We feel that there is a need to follow up the HIV-negative subjects with abnormal scores to determine the significance of these scores in this subgroup. At the time of this study, it was not possible to administer a full battery of neuropsychological tests to the study subjects. Our aim at this phase of our study plan was to determine the usefulness of the IHDS that has been shown to have an acceptable level of sensitivity as a screening tool for HAD.[16] However, the current study is looking at this very study sample, subjecting them to a complete set of neuropsychological tests by certified neuropsychologists, to determine the real prevalence of HAD and HACI.

Our data demonstrate that this rapid IHDS screening tool, with very simple adaptation (translation into French), can well be used in the Cameroonian HIV population in Yaoundé to determine those at risk for potential HAD/HACI. The test can be easily administered by a trained non neurologist. On the average, the test took 5 minutes to complete in our study. It identified the population of HIV subjects at risk for potential HAD/HACI who would need a further complete neuropsychological battery of examinations for confirmation. We do recognize that this test does not replace the neuropsychological tests for diagnosing HAD, but it is useful in directing limited resources for the diagnosis of HAD/HACI to those at risk for developing this complication and therefore seems to be quite suitable for resource-limited countries like Cameroon. We therefore suggest that all studies in HAD in Cameroon should start with the IHDS as a screening tool as a strategy for minimizing costs and increasing efficiency in patient management and disease control.

CONCLUSIONS

We have successfully used the IHDS for the first time to screen for the risk of HAD/HACI in Yaoundé—Cameroon. The mean total score and the alternating hand sequence and word recall tests are more useful elements in distinguishing between HIV patients at risk and normal healthy subjects. We suggest that all studies in HAD in Cameroon should strategically start with the IHDS as a screening tool.

HAD/HACI seems to be an important complication of HIV infection in Yaoundé—Cameroon, with a potential risk prevalence of 21.1%. Studies are currently underway to confirm these results using a full battery of neuropsychological tests. If confirmed, the IHDS will become a very useful public health screening test for HAD/HACI in Cameroon.

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