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Original Research Article

Cognitive and Mood Impairment among HIV Seropositive Patients in A Special Treatment Clinic

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Abstract: The prevalence of Human immunodeficiency virus (HIV) associated neurocognitive disorder is increasing worldwide despite the widespread use of antiretroviral therapy. Mood disorders are also widely reported among HIV seropositive patients. Cognitive and mood disorders are associated with poor drug compliance and worsening morbidity and mortality among HIV seropositive patients. Frequency of cognitive impairment ranges from 30 to over 45% in different reports. Studies have reported a frequency of depression greater than 50% in a cohort of patients. We conducted a Cross-sectional study which enrolls one hundred and twenty six HIV seropositive patients visiting a special treatment clinic. Cognitive function was assessed using the community screening instrument for dementia (CSID) and Trail making test A (TMTA). Anxiety and depression was assessed using the Hospital Anxiety and Depression Scale (HADS). The mean age of the participants was 39.1 (8.87). We observed a male to female ratio of 2:1. All subjects had at least a primary school education. The prevalence of cognitive impairment based on CSID and TMTA was 19.6% and 19.8% respectively. Based on HADS 7.9% had borderline anxiety; 4.8% had anxiety; 5.6% had borderline depression, while 4.8% were depressed. We also an inverse relationship between cognitive function and the age of the patients (t= -2.35; p=0.024). Our study observed a high prevalence of cognitive impairment among HIV seropositive patients in the special treatment clinic.
Keywords: Cognitive function, Anxiety, Depression, Human Immunodeficiency Virus.

INTRODUCTION

The prevalence of human immunodeficiency virus (HIV) associated neurocognitive disorder (HAND) is increasing despite the use of antiretroviral therapy (ART) [1, 2]. Cognitive impairment in HIV patients has been associated with poor drug compliance and increased mortality [3]. Multiple mechanisms have been suggested as causative factors for the persistence of cognitive disorder despite the use of ART that has greatly reduced the occurrence of other neurological complications of HIV. Some of the reasons proffered include: irreversible brain damage before commencement of ART; incomplete viral clearance in the brain owing to the poor central nervous system (CNS) penetration or presence of drug resistant viral strains; neurotoxicity of antiretroviral drugs and exposure to other factors which are known to cause cognitive impairment in the general population such as amyloid pathology and vascular risk factors [4]. For purposes of research, HAND has been classified in order of increasing severity into asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV-associated dementia (HAD) [5]. HAD correlates with a low CD4 count and a high viral load, advanced clinical stage of disease and low haemoglobin concentration [6, 7].

Cognitive impairment in HIV patients involves changes in concentration and attention; mental slowing; word-finding difficulties; impaired executive functions, dysfunction in short-term and working memory, and abnormalities of motor coordination. The prevalence of cognitive impairment at the different stages of HIV infection using the center for disease control (CDC) staging has been reported as 36%, 40% and 45% for stages A, B, and C respectively [4]. A Study from Northern Nigeria [8], reported symptomatic HAND in 40% patients of ART naïve patients and in 30% of patients on ART.

Sacktor *et al*. [9], in a multicenter cohort study, observed a frequency of HANDS ranging between 25-31% between 2007 to 2013. Their study enrolled patients with mean age, CD4 count and years of HIV infection of 47.4 (8.9); 589 (278) and 11.2 (7.9) respectively. A case control study observed a prolongation of the visual and auditory reaction times, computerized visual scanning task time and binary

choice reaction times, among the HIV group compared to healthy controls (p=0.05) [10]. Among the factors that have been found to predict cognitive impairment in HIV includes imaging findings severity of cerebral atrophy and basal ganglia changes and total amount of tau level in the cerebrospinal fluid (CSF) analysis [4].

Although HIV Dementia scale (HDS) is the most widely used tool in HIV seropositive patients for the assessment of cognitive impairment owing to the ease of its use, computer-based instruments have been observed to reduce the time burden of patient evaluation on the researchers. However, using a combined set of test batteries has demonstrated a superior performance when compared to HDS [11, 12].

Mood disorders occur widely among patients living with HIV/AIDS [13, 14]. The presence of anxiety and depression in patients with HIV/AIDS poses a major challenge to effective management of patients and it is a major cause of worsening morbidity and mortality [13, 14]. Studies within and outside the sub-Saharan sub-region have reported very high frequencies of mood disorders in HIV seropositive patients. In a multicenter cohort study [9], with a mean age of participants being 47.4(8.9) and mean CD4 of 589 (278), the frequency of HANDS ranged at different times between 25-31%. Another cohort study that lasted for 8 years involving 1809 volunteers recorded a 21.3% prevalence rate of depression. The study also observed that lower CD4 counts were found among depressed participants compared to the non-depressed ones [15]. A report from Indian which utilized the Centre for Epidemiologic Studies Depression scale (CES-D) to evaluate people living with HIV for depression, observed a 58.75% frequency of depression among patients on ART. The observed frequency increases with increasing severity of illness, being unmarried and unemployed [13]. Tesfaw et al. in Ethiopia reported a prevalence of anxiety and depression of 32.4% and 41.2% respectively [14].

Aims and Objectives

We evaluated cognitive impairment among HIV seropositive adult subjects attending the special treatment clinic (STC) of University of Calabar Teaching Hospital (UCTH). The specific objectives were to determine the prevalence, pattern and predictors of HIV associated neurocognitive disorder (HAND) amongst our study population.

METHODOLOGY

This Cross-sectional study enrolls one hundred and twenty six HIV seropositive patients visiting a special treatment clinic. We enrolled HIV seropositive patients 18 years of age and above presenting at the STC. Both subjects who were ARV naïve and those on ART were all recruited. Patient who refuse to consent for the study and those with a previous history of stroke or head injury were excluded.

Two multi-domain neuropsychological tests battery comprising of the Community Screening Instrument for Dementia (CSID) and Trail Making Test (TMT) were used to assess cognitive function. These are instruments have been validated and used widely in similar settings in previous studies [16,17]. Presence of mood disorders was assessed using the hospital anxiety and depression scores (HADS) and the demographic information of patients was obtained using a standardized questionnaire. Cognitive performance of all study subjects was correlated with patients' demographic and routine laboratory parameters from their hospital records to determine the possible predictors of HAND.

Patients were categorized based on TMTA as having cognitive impairment if the time they used to complete the trail making task is more than 78 seconds which is the established cut-off point for this test instrument by the original authors of the instrument and subsequently validated in studies in our environment [17-19]. Using CSID the cut-off point for cognitive impairment is fixed at a total CSID score less than 45 which is two standard deviation below the mean of normal for this population obtain in a pretest of normal subjects. CSID is a cognitive screening instrument which has been widely used in several studies among different patient populations in Nigeria [20-22].

Ethical approval

Ethical approval for this study was obtained from the ethical committee of the University Teaching Hospital where this study was conducted. The study was conducted using the guidelines provided by the ethical committee of this hospital.

Data analysis

Statistical Package for Social Science (SPSS) software version 22 was used to analyse the data from this study. Our observations are presented in form of prose, table and figures. Categorical data are shown as frequencies and proportions, while numerical data are presented as means and standard deviation. The mean scores of among the HIV seropositive group were compared with that of controls using student t-test. Significant level was set at p value < 0.05.

RESULTS

Our study recruited 126 consenting HIV seropositive patients with a mean age of 39.1 (8.87), 93 of them (73.8%) were aged <45 years while only 3 subjects (2.4%) were older than 65 years. The male to female ratio was 2:1. All subjects had at least 6 years of primary education with 102 subjects (80.1%) already involved in some form of tertiary education. The demographic details are shown in table 1.

The mean laboratory parameters of our subjects are presented in table 2. The mean CD4 count the patients was 488.9 (295.68); alanine aminotransferase was 28.1 (17.13) and haemoglobin was 13.2 (9.69).

Regarding ART use, only 2 patient (1.6%) were not on treatment with ART. Among the patients currently being treated with ART, 58 subjects (46.0%) had used ART for 1 to 5 years, while 59 subjects (46.8%) have been on ART for > 5 years. This is shown in table 3. The number subjects with cognitive impairment based on CSID score was 24 (19.0%) while that based on TMTA was 25 (19.8%). This is represented in table 4. From tables 5, 6 and 7 only the age of the subjects had an inverse relationship with their cognitive performance (t-test=-2.35; p value= 0.024). This is further confirmed by the linear correlation between both variables in table 7 (p value =0.019).

There was no significant difference in cognitive function between patients who had used ART for less than 5 years (N=67) and those who have used it for more 5 years (N=59) based on CSID (95% CI = -4.127- 0.929; p =0.868) and TMTA (95% CI = -9.588 – 14.388; p = 0.396).

The prevalence of anxiety and depression among this cohort of HIV seropositive patients is as shown in figure 1 and 2 below. The mean CD4 count among the participants in depression, borderline depression and normal category were 303.5 (219.6); 409.3 (357.4) and 503.6 (293.5) respectively. Although the depressed patients had lower CD4 count, this difference was not statistically significant (p=0.655).

Table-1: Socio – demographic characteristics of study participants

Variable	Frequency (N = 126)	Percentage (%)
Sex		
Male	84	66.7
Female	42	33.3
Age category (years)		
Young (<45)	93	73.8
Middle age (45-65)	30	23.8
Elderly (>65)	3	2.4
BMI category (kg/m^2)		
< 18.5	2	1.6
18.5 – 24.9	63	50.0
25.0 – 29.9	47	37.3
30 & above	14	11.1
Educational status		
No formal education	0	0.0
Primary	4	3.1
Secondary	20	15.9
Tertiary	102	80.1
Marital status		
Married	73	57.9
Single	30	23.8
Divorced	3	2.4
Separated	4	3.2
Widowed/widower	16	12.7
Alcohol use		
Yes	17	13.5
No	109	86.5
Tobacco use		
Yes	2	1.6
No	124	98.4

Table-2: Mean demographic and laboratory characteristics of patients

Variable (N=126)	Mean (SD)
Patients Age	39.1 (±8.87)
Systolic Blood Pressure	114.1 (±16.35)
Diastolic Blood Pressure	72.8 (±10.53)
BMI of Patients	31.22 (±10.63)
Haemoglobin	13.2 (±9.69)
CD4 count	488.9 (±295.68)
Alanine Aminotransferase	28.1 (±17.13)
Aspartate Aminotransferase	25.4 (±15.68)
Creatinine Clearance	80.62 (±38.89)

Table 3: Duration of HIV Diagnosis and ART Use

Variable	Frequency (N = 126)	Percentage (%)
ART use		
Not on ART	2	1.6
On ART	124	98.4
Duration of ART use		
<3 months	3	2.4
3-6 months	1	0.8
6 -12 months	5	4.0
1 year to 5 years	58	46.0
> 5 years	59	46.8
Duration of HIV diagnosis		
<3 months	2	1.6
3-6 months	1	0.8
6 months to 1 year	7	5.6
1 year to 5 years	56	44.4
>5 years	60	47.6

Table-4: Prevalence of cognitive impairment based on TMTA and CSID

Variable	Frequency (N = 126)	Percentage (%)
Based on TMTA		
Cognitive impairment	25	19.8
No cognitive impairment	101	80.2
Based on CSID		
Cognitive impairment	24	19.0
No cognitive impairment	102	81.0

Table-5: Predictors of cognitive impairment using the TMTA score

Variable	t-test	Unadjusted coefficient (95% CI)	P-value
Age	-1.92	-7.58 – 0.06	0.053
Systolic blood pressure	-1.85	12.18 – 0.51	0.07
Diastolic blood pressure	-0.62	-1.53 – 2.47	0.51
BMI	1.14	-5.07 – 18.69	0.26
Haemoglobin	1.01	-1.09 – 3.35	0.32
CD4 count	-0.16	-145.94 – 124.59	0.87
Alanine Aminotransferase	1.75	-0.64 – 9.88	0.84
Aspartate Aminotransferase	-0.82	-11.22 – 4.76	0.42
Creatinine Clearance	-1.20	-44.14 – 11.52	0.239

Table-6: Predictors of cognitive impairment using the CSID score

Variable	t-test	Unadjusted coefficient (95% CI)	P-value
Age	-2.35	-8.01 – 0.59	0.024
Systolic blood pressure	-1.18	-12.81 – 3.43	0.25
Diastolic blood pressure	-0.66	-7.04 – 3.61	0.516
BMI	1.07	-5.45 – 18.11	0.289
Haemoglobin	1.11	-0.96 – 3.41	0.27
CD4 count	-0.41	-156.14 – 184.18	0.69
Alanine Aminotransferase	0.35	-5.60 – 7.92	0.73
Aspartate Aminotransferase	-0.86	-11.82 – 4.81	0.40
Creatinine Clearance	1.68	-1.77 – 20.96	0.097

Table-7: Correlation analysis clinical/biochemical parameter/TMTA score with the CSID score

Variable	Pearson correlation	P-value
Age	-0.209	0.019
Systolic Blood Pressure	-0.039	0.663
Diastolic Blood Pressure	-0.023	0.798
BMI	0.010	0.910
Haemoglobin	0.117	0.193
CD4 count	-0.016	0.863
Alanine Aminotransferase	0.035	0.698
Aspartate Aminotransferase	-0.022	0.810
Creatinine Clearance	0.023	0.795
TMTA Time	-0.345	0.000

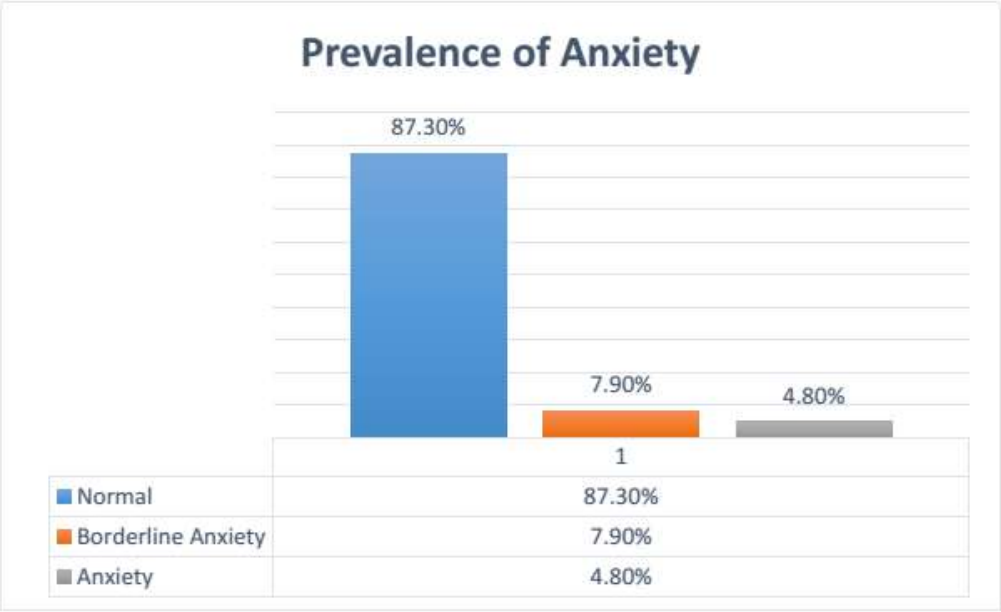

Fig-1: Prevalence of Anxiety

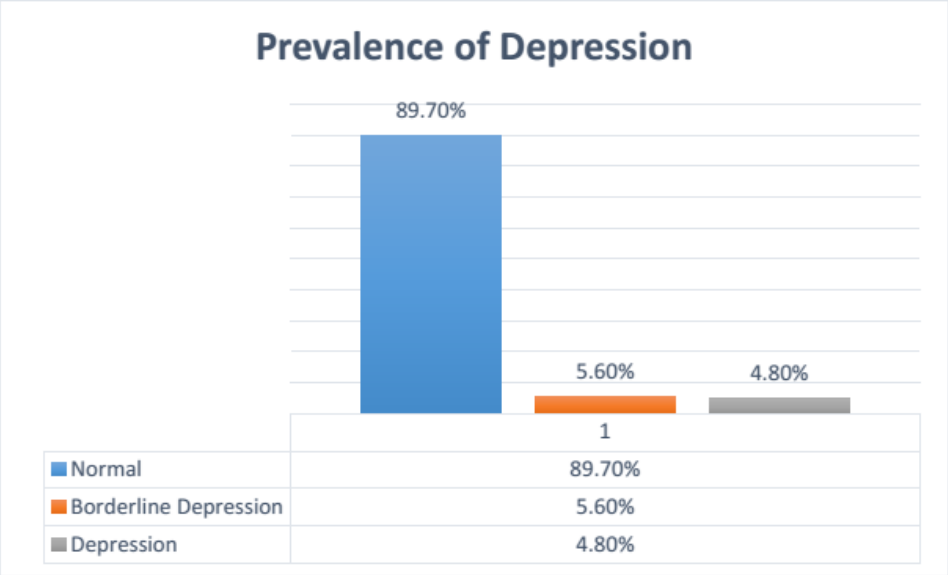

Fig-2: Prevalence of Depression

DISCUSSION

Our study observed a prevalence rate of cognitive impairment of 19.8% and 19.0% based on TMTA and CSID. This prevalence rate was lower than that was previously reported in previous studies.

The mean haemoglobin of our study participants was 13.2 (9.69) is relatively high and that might be because almost all them were on ART which is co-administered with haematinics. The relatively high mean CD4 count of 488.9 (295.68) might be due to the fact that over 40 % of our enrolled patients had been on ART for more than 5 years.

The observed lower prevalence of anxiety (4.8%) and depression (4.8%) in our study compared to higher frequencies in similar studies [9,15,13], might be due to difference in methodology and screening instruments used in these studies. If the participants in our study who were among the borderline category were combined with those under the depression or anxiety group the prevalence will be 12.7% for depression and 10.4% for anxiety respectively. These rates are closer to that obtained in previous studies.

The difficulty in determining predictors of cognitive impairment or mood disorders among our patients might be due to the fact that these patients have benefitted from well-structured psychological and pharmacological interventions. Higher prevalence figures could have been obtained if these patients were recruited at initial presentation in the STC.

Conclusions and Limitations

Cognitive impairment is common among HIV seropositive Nigerians. Increasing age is a strong risk factor for cognitive impairment among people living with HIV.

We were unable to compare cognitive function among equal numbers of demographically match ART naïve patients and those on treatment, to determine the impact of treatment on their cognitive function. We could not also explore the relationship between cognitive function and viral load in this study. We were unable to carry out any form of cranial imaging for these patients to rule out a coexisting silent infarct.

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