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Neurological manifestation with special reference to HIV-associated neurocognitive disorder (HAND) among people on anti-retroviral treatment in India

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Abstract. – OBJECTIVE: The neurological manifestations and their severity in patients on antiretroviral treatment (ART) are currently unexplained. We aimed at studying the prevalence of HIV Associated Neurological Disorders (HAND) among people on antiretroviral treatment, using the International HIV Dementia Scale (IHDS).

PATIENTS AND METHODS: A predesigned and pretested proforma including the International HIV Dementia Scale (IHDS) was administered to 100 HIV patients attending to ART center of KIMS teaching Hospital (Koppal, Karnataka) from January 2020 to March 2020. The data was analyzed SPSS version 15 software. Descriptive statistics were used for demographic characteristics. The Student's t-test and chi-square test methods were applied to determine the relationship between qualitative characteristics.

RESULTS: The prevalence was found to be 59%. Out of 100, 57 HIV patients scored less than 10 whereas 43 HIV patients scored ≥10 on the IHDS scale. The mean age of the study population was 39.14 ±13.01 years; the total IHDS score was 9.96±1.53 and the CD4 count was 427.91±226.0. This study demonstrated that the patients with CD4 count more than 350 (i.e., 63.60%) had a better IHDS score.

CONCLUSIONS: Neurocognitive disorder was found to be more common than anticipated. All ICTC Centers need to consider assessing HIV-associated neurocognitive disability (HAND), and the International HIV Dementia Scale (IHDS) as one instrument for such assessment.

Key Words:
Human Immuno-deficiency Virus (HIV), International HIV Dementia Scale (IHDS), HIV associated neurocognitive disorders (HAND).

Introduction

HIV remains the most feared infection of the twenty-first century due to the difficulty of finding an effective cure for the disease. The initiation of ART to people with HIV has led to the prevention of a possible "medical apocalypse." Strict adherence to ART helps to reduce the viral load and hence delays the onset of AIDS, ensuing a prolongation life expectancy that is close to average. Despite the introduction of ART, many patients fail to comply due to possible adverse side effects of medications or due to drug abuse, psychiatric disorders, socioeconomic conditions, educational status, and social stigma. To overcome the obstacles, close supervision, significant social changes, and effective counseling must be enforced.

Human Immunodeficiency Virus (HIV) is considered a neurotrophic virus invading the brain directly and producing varied neuropsychiatric manifestations. The commonest manifestation described is AIDS dementia complex, otherwise labeled as HIV Associated Dementia (HAD)[1]. According to the Frascati criteria, HAD is described as impairment in at least two cognitive

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domains, scoring at least two standard deviations (SD) below demographically appropriate means, with marked impairment of activities of daily living (ADL) caused by the cognitive deficits[2]. Previous reports revealed that the routine asymptomatic screening of HAD remains challenging due to the complexity of diagnosis. Currently, certain screening scales[2,3-11] and computerized batteries of tests[12,13] are in practice for the diagnosis; however, there are not enough literature reports available for their accuracy. The HIV Dementia Scale (HDS) and the International HIV Dementia Scale (IHDS) are two rapid tests for HAD, and further evaluation is required for those who are found to have neurological manifestations by either the HDS or the IHDS scales[14,15].

The HDS published in 1994, has been the first screening method for HIV-associated dementia. Several other screening methods have been suggested since then. Due to various differences in population groups, geographical variations, and socioeconomic factors, there is no uniformly applicable screening tool that can provide the highest level of reliability. The IHDS was designed as a short, cross-cultural screening method for identifying people at risk of HIV dementia worldwide. IHDS takes less than five minutes to prescribe and can be done by doctors who lack training in identifying advanced neurological conditions. Hence, the IDHS can be applied to patients attending any primary care facility.

Major cognitive deficits have been identified in India in individuals with advanced HIV disease and not initiated on Highly Active Antiretroviral Therapy (HAART)[16]. Cognitive disability has been found in at least two domains in people living with HIV/AIDS (PLWHA)[17]. Asymptomatic HIV infections leading to neurocognitive impairments have been a focus of research due to their potential impact on work-related performance. Cognitive impairment has been identified to be around 60% to 90% among asymptomatic HIV patients[18,19]. Recent studies indicate that neurocognitive dysfunction worsens with deteriorating health status[20]. With this context, the current research used the IHDS to assess the prevalence of HAND among people on antiretroviral treatment at a medical teaching hospital in India.

Patients and Methods

This cross-sectional study was conducted in a Medical College Teaching Hospital in North Karnataka, India, at the Integrated Counselling and Testing Centre (ICTC). A predesigned and pretested proforma including the IHDS was used to collect information. The ICTC counselors were selected as data collectors because of better relationship with the patients. They were oriented regarding the objectives of the study and trained to use the IHDS scale to test for dementia.

The study's participants were HIV-positive patients who attended the KIMS Teaching Hospital's HAART center. HIV-positive patients who were more than 18 years and on HAART for a period of a minimum of one year were included in the study. The proposed research was accepted by the Ethical Committee at KIMS Teaching Hospital. Before the evaluation began, each participant signed an informed written consent form as proof of their willingness to participate in the study. A permission letter from the Integrated Counselling and Testing Centre (ICTC) nodal officer at the Medical College Hospital and Research Centre was obtained to conduct the report. Requisite permissions were also obtained from the District AIDS Prevention Officer, and District AIDS Prevention and Control Unit all gave their approval. Furthermore, confidentiality was maintained by limiting reports on test results to the ICTC counselor alone. The counselors administered the IHDS scale after gathering baseline information from the patients.

The IHDS consists of three items: (1) memory recall of four items in two minutes, (2) testing for motor speed, and (3) testing for psychomotor speed. Each item contributes 4 points to the total score of 12. Administration requires approximately 10 minutes. The IHDS showed a sensitivity of 80% and specificity of 57% at the cut-off score of less than or equal to 10[21]. The IHDS has been tested and validated for use in Indian settings by Muniyandi et al[22] in 2012. Individuals scoring less than ten were considered to be having dementia and were referred to ICTC Medical Officer for further confirmation of diagnosis and management.

Statistical Analysis

Version 15 of Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) software was used to analyze the data. For each variable, descriptive statistics were computed. To determine the relationship between cognitive impairment and the variables, the chi-square test, and Student's *t*-test were used. For categor-

Table I. Descriptive Statistics of Study Population.

		Mean	S.D.	95% confidence interval
Age (in years)		39.14	13.01	36.56-41.72
IHDS	Motor	3.25	0.77	3.10-3.40
	Psychomotor	2.95	0.93	2.76-3.14
	Memory	3.76	0.50	3.67-3.86
	Total	9.96	1.53	9.65-10.27
CD 4 count (per cu. mm)		427.91	226.0	383.07-472.75

ical variables, the chi-square test was used to assess associations with cognitive impairment. A two-tailed *p*-value less than 0.05 was considered significant.

Results

Among 100 HIV-positive patients who attended the HAART center of KIMS teaching Hospital, Koppal, Karnataka, the mean age of the study population was 39.14 ±13.01 years; the total IHDS score was 9.96±1.53, and CD4 count was 427.91±226.0. The descriptive statistics of the study population are represented in Table I.

A total of 57 study subjects attended the HAART center of KIMS teaching Hospital, Koppal, Karnataka, scored less than 10, whereas 43 HIV patients scored ≥10 on the IHDS scale. There was a significant age-wise distribution of IHDS score was observed among the HIV-positive patients. In all the age groups, the majority of individuals had IHDS score less than 10 except between 11 to 20 years, where the majority scored ≥10. It was observed from our study that the patients with CD4 count more than 350 (i.e., 63.60%) and had a better IHDS score as compared to those with a low CD4 count. The relationship of socio-demographic characteristics of the participants and the IHDS score was represented in Table II.

The IHDS scoring pattern in the majority of the study participants had a good overall IHDS score. Forty-five individuals were able to perform 15 timed motor skills in 5 seconds; 33 individuals were able to perform four psychomotor sequences in 10 seconds, and 74 individuals were able to recollect all four words for memory recall. The IHDS scoring pattern of HIV-positive patients is depicted in Table III.

Discussion

Studies conducted in India have reported a varied prevalence of dementia ranging from 32.50% to 67.50%. The prevalence of dementia in the present study was found to be 59%. In a study conducted by Muniyandi et al[22], 63.60% of study population scored positive on the IHDS scale. Of the three subsets of the scale, the alternating HAND sequence test was the most sensitive and was abnormal in 63.60% of the study population.

Table II. Age and Gender Wise Distribution of IHDS Score.

		Total score					
Parameter		< 10 No. (%)	≥ 10 No. (%)	Total No. (%)	χ^2	df	*p*
Age (years)	11-20	1 (10.0)	9 (90.0)	10 (100.0)	12.37	4	0.015
	21-30	10 (58.8)	7 (41.2)	17 (100.0)			
	31-40	19 (63.3)	11 (36.7)	30 (100.0)			
	41-50	16 (61.6)	10 (38.5)	26 (100.0)			
	≥ 51	13 (76.5)	4 (23.5)	17 (100.0)			
Gender	Male	33 (57.9)	24 (42.1)	57 (100.0)	0.67	1	0.796
	Female	25 (60.5)	17 (39.5)	43 (100.0)			
CD 4	Less 350	27 (40.3)	40 (59.7)	67 (100.0)	0.14	1	0.704
	≥ 350	12 (36.4)	21 (63.6)	33 (100.0)			
Total		57 (57.0)	43 (43.0)	100 (100.0)			

Table III. IHDS Scoring.

Parameter	Category	Frequency	Percentage (%)
Motor	7-10 in 5 seconds	20	20.0
	11-14 in 5 seconds	35	35.0
	15 in 5 seconds	45	45.0
Psychomotor	1 sequence in 10 seconds	8	8.0
	2 sequences in 10 seconds	22	22.0
	3 sequences in 10 seconds	37	37.0
	4 sequences in 10 seconds	33	33.0
Memory	One word	1	1.0
	Two words	2	2.0
	Three words	10	10.0
	Three words with clue	13	13.0
	Four words	74	74.0
Total		100	100.0

Another study reported a relatively small range of ages infected with HIV in the study sample; age had an adverse effect on the performance on the IHDS scoring system[23].

The neurocognitive impairment was found to be higher among women (66.70%) compared to men (42.90%) with a *p*-value-0.01; the odds ratio (OR) was 2.66, with a 95% confidence interval (95% CI) of 1.22-5.82. No statistically significant difference of cognitive impairment (IHDS 10) was identified between women aged 40 (68.30%) and more than 40 years (57.10%) *p*-value-0.67. Neurocognitive impairment was more common in patients over 40 years old (61%) than in patients under 40 years old (35.30%), OR 2.87 (95% CI 1.24-6.64). Twenty-five percent of female respondents (60.50%) and 33% of male respondents (57.90%) tested positive for dementia, which was not found to be statistically significant. Nakku et al[24] also reported similar findings in a study conducted among the African population.

A lower CD4 cell count was found to have an increased likelihood of cognitive dysfunction in a study conducted by Heaton et al[25] in rural China. Similar findings were also included in the current study's findings. Troncoso et al[26] also reported an increased prevalence of neurocognitive impairment among PLHWA with low CD4 levels. A recent CD4 count of less than 200 cell/mm^3 was associated with a higher rate of IHDS 10 than those with a recent CD4 count more than or equal to 200 cell/mm^3, but the difference was not statistically important (88.80% *vs.* 50.0%, respectively, OR 8.0, 95% CI 0.96-66.3)[26]. McCombe et al[27] found that as age advanced, the prevalence of HAND increased in a longitudinal cohort sample in Canada. In a multivariate study, the authors found that after the age of 18, the risk of developing HAND increased by 3.20% with each additional year of age. The authors also discovered a connection between HAND and high viral load, a low CD4, and the length of HIV infection[7].

Variation in prevalence of HAND greatly depended on the source consulted[28,29]. The prevalence was found to range from 69% to 79% in a cohort of HIV-positive people in French-speaking Zurich. Among men who have sex with men in the London metropolitan area, the prevalence of HAND was found to be 21 to 30%[29]. These variations can be attributed to gender, age, educational level, comorbidities, and viral control between the study groups[31]. Age and Education were found to have a consistent correlation with HAND. The findings have been confirmed by other studies conducted earlier[7,32,33].

This study was single-centric with limited sample size. Specific variables of the participants, such as previous periods of psychological disturbances, substance abuse, also serve as diagnostic confounders. Nevertheless, the use of IHDS helped to refer patients to a neuropsychological examination that verified an asymptomatic neurocognitive condition without obvious clinical anomalies. One single, self-reported complaint scale was used to assess cognitive dysfunction. All of the responses were dichotomous, which may have restricted the amount of knowledge collected, despite its widespread use in the analysis. Patients with advanced illness may lack the ability to provide a reliable answer to self-reported questionnaires since they will be unaware of their worsening condition. Hence, patient can be misclassified as asymptomatics due to doubtful condition of their true symptoms.

Conclusions

According to the findings of the current study, the prevalence of HAD was higher as per the IHDS criteria. Since many of these study subjects were on treatment with HAART, the occurrence neurocognitive impairment is a matter of concern. Further confirmation of diagnosis can be done using other battery of tests and other population groups.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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