Cognitive Impairment among Persons of Rural Background Living with Human Immunodeficiency Virus Infection on Antiretroviral Therapy: A Study from a Tertiary Care Centre of North India

Sir,

Human immunodeficiency virus (HIV) infection is often accompanied by progressive neuropsychiatric manifestations varying between asymptomatic neurocognitive impairment, mood and personality disorders, psychosis, mild cognitive-motor disorder, and HIV-associated dementia (HAD).^[1,2] Since it adversely affects adherence to medications, interact socially or ability to work, and employability, early

recognition and management of individuals with HAD are important for improving quality of their life.^[3,4] However, it remains understudied despite a significant prevalence of HIV/AIDS-affected Indian populations.^[5-7]

We studied 356 (male:female 154:202) HIV/AIDS-affected persons (old and new) aged 10–79 (mean $\pm$ SD = 39.67 $\pm$ 9.88) years between July 2015 and June 2016 presenting in the dermatology outpatient clinic and institutional antiretroviral

Table 1: The Bharmour Mental State Examination scale^[8] used for assessment of cognitive impairment

Maximum score	BMSE
5	What is the time of day? day, date, month, and season
5	Where are we now: country/state/district/block/panchayat
3	The examiner names three unrelated objects in native (Bharmouri) language clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5	We constructed a story for the subtraction task: "You went to a grocer with a fifty rupees note to make a purchase of seven rupees. After paying him how much will be left with you? In the next morning you went again to purchase the same item, how much will be left with you?" The first five consecutive responses are scored
	World backward. Since most of the sample is illiterate, spelling (either forward or backward) is not an option. We ask subjects to name the months in Hindu calendar backward, starting from the current month. Responses were scored for the 5 months named, not including the current month. This was thought as closest possible to "world backward" option in capturing attention of the subjects
3	Earlier, I told you the names of three things. Can you tell me what those were?
2	Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them
1	Repeat the phrase with: now, when, then as focus
3	Take the paper in your right hand, fold it in half, and put it on the floor (the examiner gives the patient a piece of blank paper)
1	The examiner says, "just see what I am doing and repeat the same" and then closes his own eyes for 3 s (follow example) and later examiner observes the subject (see and follow command)
1	A meaningful sentence generation in response to the question by the examiner
1	Please copy this picture (the examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below)

30	Total

Interpretation of score: (1) Maximum score = 30, (2) Score ≥ 24 = Normal, (3) Score between 18 and 23 = Mild dementia (4) Score < 18 = Moderate to severe dementia. BMSE: Bharmour Mental State Examination

therapy (ART) center. Their sociodemographic details, CD4 counts, and presence of any other illness were recorded from individual's highly active ART (HAART) records and clinical examination. All enrolled subjects completed a predesigned questionnaire with investigators' help in their native language [Table 1]. This pretested questionnaire to suit Indian patients is structured for assessing the dementia status of HIV/AIDS-affected persons using Bharmour Mental State Examination (BMSE) scale.^[8]

The clinicoepidemiologic profile of the study population [Table 2] was similar as reported previously^[9] and comprised majority, 235 (66%) in 31–45 years age group. The 336 (94.4%) ruralites made the majority and 206 (56.9%) persons were either school dropouts, illiterate, or under matric. Most, 121 (34%), individuals were drivers, staying-alone laborers, and self-employed among males and 196 (55%) women were homemakers. The 22 (6.2%) children/adolescents (16 boys, 6 girls) aged 10–19 years were students. The mode of infection was heterosexual in 335 (94.1%) individuals. The majority, 340 (95.5%) persons, were in WHO stage-1 of HIV disease.^[10] All (100%) were on regular HAART for 1 month to 9 (mean 3.5) years and CD4 counts ranged from 100 to 350 cells/mm³ in 142 (39.9%), > 500 cells/mm³ in 136 (38.2%), and < 100 cells/mm³ in 78 (21.9%) individuals, respectively.

Only 3 (0.8%) persons were identified having mild dementia/neurocognitive impairment on BMSE scale; a 10-year-old school-going boy (Score: 22), a 38-year-old self-employed man (Score: 22), and 31-year-old woman (Score: 23). They had WHO clinical stage-1 of the disease, were under matric, on regular HAART (tenofovir, efavirenz,

lamivudine) for 6 months, 4 years, and 5 years, respectively, which was started a month after clinical diagnosis. They had CD4 counts of 173, 190, and 179 cells/mm³, respectively.

HAD, a phenotype of HIV-encephalitis, earlier known as AIDS dementia complex (ADC), is attributed to the virus-infected brain macrophages and activated microglia in the central nervous system. HIV-associated neurocognitive disorder is the new definition for ADC and considered AIDS-defining illness. It was not uncommon having an estimated incidence of 10% before the introduction of HAART in 1996 but has decreased approximately by 50%, since then with an estimated prevalence of 21%–80% now.^[1,11] Paradoxically, an increased prevalence of mild forms is being recognized more often than before.^[2,12] However, the overall incidence and prevalence rates of HAD in the post-HAART era vary greatly by geography, treatment, and risk factors studied.^[13] Old aged HIV + individuals are definitely at higher risk for HAD than HIV-seronegative individuals.^[14,15] High viral load during early stage, female gender, family history of dementia, depression, low educational level, unemployment, low CD4 counts (nadir CD 4 count 50 cells/mm³), anemia, systemic symptoms, and intravenous drug abuse are other identified risk factors for HAD in studies but included no Indian populations.^[2,11,16–19] Good education suggests a cognitive reserve and mind's resiliency to neuropathological damage while HIV/AIDS-affected individuals with lower cognitive reserve have demonstrated worse neuropsychometric performance.^[19] This is also evident in our 3 (0.8%) patients with signs of mild HAD having low education status, the only identified risk factor in them. However, we did not study HIV viremia in them.

Table 2: Baseline characteristics of patients

Baseline characteristics	Total number of patients studied, <i>n</i> =356 (%)	Patients with cognitive impairment (<i>n</i> =3)
Gender		
Men	154 (43.3)	2
Women	202 (56.7)	1
Men: women	1:1.3	-
Age (years)		
Range (mean±SD)	10-79 (39.67±9.88)	
<15	6 (1.7)	1
16-30	37 (10.4)	-
31-45	235 (66.0)	2
46-60	72 (20.2)	-
>60	6 (1.7)	-
Social background		
Married	274 (76.9)	2
Unmarried	24 (6.7)	1
Widowed	55 (15.4)	-
Divorced	3 (0.8)	-
Rural	336 (94.4)	-
Urban	20 (5.6)	-
Education status		
Under 10 th standard/school drop outs/illiterates	206 (56.9)	3
10 th standard or more	150 (42.2)	-
Occupation		
Men		
Drivers	72 (20.2)	-
Laborers	20 (5.6)	-
Self-employed	29 (8.1)	1
Government employed	15 (4.2)	-
Defense personnel	2 (0.6)	-
Students	16 (5.5)	1
Women		
Homemakers	196 (55.0)	1
Students	6 (1.7)	--
Mode of disease acquisition		
Heterosexual	335 (94.1)	
Mother to child (vertical)	17 (4.8)	-
Blood transfusion	3 (0.8)	-
Injections	1 (0.3)	-
CD4 cell counts, <i>n</i> =356 (cells/mm ³)		
>500	86 (24.2)	-
>350-500	50 (14.0)	-
>200-350	48 (13.5)	1
Range 6-1254 (cells/mm ³)		
>100-200	94 (26.4)	2
<100	78 (21.9)	-
Clinical stage (WHO 2007) ^[9]		
Stage 1	340 (95.5)	3
Stage 2	12 (3.4)	-
Stage 3	4 (1.1)	-
Stage 4	0	-
Time interval between diagnosis and initiating ART		
Range (mean)	1 day to 13.5 years (383.13 days)	0-10 days
Duration of ART		
Range (mean)	1 month to 9 years (3.5 years)	1 month to 2 years

ART: Antiretroviral therapy, WHO: World Health Organization, SD: Standard deviation

Although several screening tools have been used to identify cognitively impaired individuals in HIV outpatient clinics, the International HIV Dementia Scale remains popular internationally.^[14,15,20-22] Indian studies have also used

similar scales;^[6,7] however, being in English, it remains under-evaluated being poorly comprehensible by Indian patients. The BMSE scale in native language used by us was convenient and easily comprehended by studied subjects.

Despite small number of subjects, lack of HIV-seronegative controls, and no viral load studies, HAD/neurocognitive impairment does not seem uncommon even among individuals on HAART. However, our results may not represent other HIV/AIDS-affected populations for being limited period, single-center, cross-sectional study. Nevertheless, an early screening for neurocognitive impairment using a formal neuropsychometric battery and identification of risk factors in Indian subjects will help in planning of comprehensive health care envisaged in Phase-IV NACP for at-risk patients.

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Conflicts of interest

There are no conflicts of interest.

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