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Original Research Article

HIV associated neurocognitive dysfunction and its association with CD4 count in HIV positive patients-a hospital based study

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ABSTRACT

Background: The main objective of the present work was to study the neurocognitive dysfunction in HIV positive patients and to determine its relation with CD4 count. Further, an attempt has also been made to study the relationship of neurocognitive dysfunction with cART regimen.
Methods: The study was a prospective observational study, conducted over a period of one year (from July 2012 to June 2013) in the Department of Medicine in collaboration with the Department of Psychiatry at Indira Gandhi Medical College and Hospital, Shimla.
Results: HIV associated neurocognitive dysfunction (HAND) was found in 39.04% patients. Mean duration from diagnosis of HIV to detection of HAND was 3.77 ± 1.7 years. Mean nadir CD4 cell count was 126.1/mm3. 39.04% patients (n=41) were found to have HIV associated neurocognitive disorder out of 105 screened patients. 95.1% patients (n=39) had asymptomatic neurocognitive impairement, 4.9% patients (n=2) had mild cognitive impairment and 2.08% patients (n=1) had HIV associated dementia. Out of 41 patients having HIV associated neurocognitive disorder, 68.3% patients (n=28) were having CD4 count less than 150. Those having CD4 count less than 150/mm3 had scored less on dementia scales indicating severe disease. 31.7% patients (n=13) were having HIV associated neurocognitive disorder (HAND) and CD4 count was more than 150/mm^3.
Conclusions: The conclusion of the study is that HIV associated neurocognitive disorder is common and asymptomatic neurocognitive impairement is the commonest type of HIV associated neurocognitive disorder in HIV positive patients. It can be detected while patient is asymptomatic with help of simple neurocognitive tests. Although few studies reported higher prevalence of HIV associated neurocognitive disorder among patients on certain combined antiretroviral therapy (cART) regimen but our study didn't indicate any such association.

Keywords: Antiretroviral therapy, CD4 count, Neurocognitive dysfunction

INTRODUCTION

Clinical disease of the nervous system accounts for a significant degree of morbidity in a high percentage of patients with HIV infection. The neurologic problems that occur in HIV-infected individuals may be either primary to the pathogenic processes of HIV infection or secondary to opportunistic infections or neoplasms. Secondary diseases of the CNS have been reported to occur in approximately one-third of the patients with AIDS.[1] Neurological involvement in HIV is often associated with cognitive impairment. The term HIV-associated neurocognitive disorders (HAND) is used to

describe such cognitive disorders. It is suggested that CD4 level correlates significantly with cognitive functioning. Once culminating in dementia in many individuals infected with HIV, HAND now typically manifest as more subtle forms of cognitive impairement and the proportion of new HAND cases occurring in patients with higher ranges of CD4 counts (200 to 350 cells) may be increasing as cART has decreased the impact of opportunistic infections.[2]

The term "HIV encephalopathy" was added to the list of those used to refer to AIDS dementia, and in 1991, the American Academy of Neurology AIDS Task Force developed definitional criteria for AIDS dementia. The terms "AIDS dementia complex," "HIV dementia," and "HIV encephalopathy," and the term, "HIV-1-associated cognitive/motor complex," which was introduced by recommendation of the American Academy of Neurology task force, are synonymous.[3] In 1991, the American Academy of Neurology defined two levels of neurologic impairment in patients with HIV: HIV-associated dementia (HAD) and minor cognitive motor disorder (MCMD). A core difference between the two is the degree of functional impairment present; patients with HAD have more impairment than those with MCMD. Due to overlap in symptoms and a lack of specificity regarding the degree of neurologic impairment necessary to make these diagnoses, a new classification system has been proposed by the HIV Neurobehavioral Research in 2007.[4]

Data from 15,380 HIV-infected patients followed in the CASCADE cohort (Concerted Action on Seroconversion to AIDS and Death in Europe) showed a decrease in the incidence of HAND from 6.49 per 1000 person-years in the pre-cART era to 0.66 per 1000 person-years by 2003 to 2006. However, the overall prevalence has remained stable.[5] HAND also accounts for an increasing proportion of AIDS-defining diagnoses. Study by Dore G. J. et al found that the proportion of AIDS cases with HAND increased from 5.2% in 1993-1995 (pre cART era) to 6.8% in 1996-2000 (post cART era).[6] In Indian studies Gupta J. D. et al on South Indian patients observed 60.5% had mild to moderate cognitive deficits.[7] None of the subjects had severe cognitive deficits.

In an observational study involving 1555 HIV-infected adults in the United States 33% had asymptomatic neurocognitive impairment, 12% had mild neurocognitive impairment, and only 2% had HIV-associated dementia.[8] In a study of patients with HIV in a Ugandan clinic, the prevalence of HAND was 31%[9]. A study by Vijay D. et al from India of 1606 HIV patients found median age of 36 years in patients with neurologic manifestations.[10] In India, Yepthomi et al reported significant cognitive deficits in advanced HIV disease in patients not receiving cART.[11] 56% of the PLWHA (people living with HIV/AIDS) were demonstrated to have impairment in at least two cognitive domains. One another study showed that 42% of subjects had HIV associated Mild Neurocognitive disorder, 1.02% had HIV associated dementia.[12] This dysfunction is more with CD4 counts less than 200. This study has shown no effect of ART on cognitive dysfunction. Gupta J. D. et al in a cohort study reported 60.5% mild to moderate cognitive deficits characterized by deficits in the domains of fluency, working memory, and learning and memory in HIV positive patients.[7] None of the subjects had severe cognitive deficits.

Leading theories of the pathologic mechanisms of neuronal damage in HIV-associated dementia involve activation of macrophages or microglial cells and/or activation of cytokines and chemokines, leading to abnormal neuronal pruning.[13] Autopsy studies of demented AIDS patients show characteristic white matter changes and demyelinization, microglial nodules, multinucleated giant cells, and perivascular infiltrate.[14] Another cofactor that may contribute to neuropathogenesis in HIV-infected patients is hepatitis C virus (HCV) infection. HCV sequences have been detected in cerebrospinal fluid and brain tissue; virus may traffic into the CNS via macrophages, which infect microglia and astrocytes. In one autopsy study of 25 HIV-infected patients with a history of neurologic impairment, nonstructural and core HCV antigens were demonstrated in brain homogenates by immunoblot analysis in 11 of 12 HIV/HCV coinfected patients. HCV core protein may cause neuronal damage through the production of proinflammatory cytokines.[15]

Although Himachal Pradesh is a low prevalence state for HIV, the number of HIV/AIDS cases are rising in Himachal Pradesh.[16] Most of the studies available in literature are done from the western countries where HIV-1 subtype B is more prevalent, showing increase in prevalence of milder forms of HAND and large proportion of new HAND cases are occurring in patients even with higher ranges of CD4 counts in post cART era, while in India including our part HIV-1 subtype C is prevalent and there is no previous study from IGMC on neurocognitive dysfunction in HIV patients.[17] The purpose of our study was to find out the neurocognitive disorders prevalent in HIV positive patients in this part of the country, its relationship with CD4 count and also to compare and to find out changes from the studies done earlier in our country.

Keeping above facts in consideration, the present work is an attempt to study the neurocognitive dysfunction in HIV positive patients and to determine its relation with CD4 count. Furthermore herein this work, an attempt has also been made to study the relationship of neurocognitive dysfunction with cART regimen.

METHODS

The study was a prospective observational study, conducted over a period of one year (from July 2012 to June 2013) in the Department of Medicine in

collaboration with the Department of Psychiatry at Indira Gandhi Medical College and Hospital, Shimla.

Inclusion criteria

The study group included the HIV positive patients of either sex attending the ART clinic/medicine OPD as well as those admitted in medicine ward from July 2012 to June 2013. Patients between 18 to 50 yrs of age were included (as age related neurocognitive decline is more likely in patients older than 50 yrs). Patients educated upto primary level of education were taken so that they can understand the and follow the commands during neurocognitive testing. Informed written consent was taken from all the patients included in the study.

Exclusion criteria

Patients having history of any major psychiatric illness, neurologic insult (stroke, tubercular meningitis, head injury), epilepsy, or those suffering from any chronic illness such as diabetes mellitus or having macrocytic anemia as folic acid and vitamin B12 deficiency can cause cognitive dysfunction; were excluded.

After selecting the patient's relevant history was taken, physical and systemic examination was conducted and the patients were subjected to Hamilton rating scale for depression (HRDS) to exclude those suffering from depression Thereafter the patients were subjected to following neuropsychological tests to assess any cognitive impairment.

Following four neuropsychological tests were used

- Mini mental state examination (MMSE)
- General practitioner assessment of cognition (GPCOG)
- International HIV dementia scale
- Montreal cognitive assessment.

1) The mini–mental state examination (MMSE) or Folstein test is a brief 30-point questionnaire test that is used to screen for cognitive impairment. A score of less than 24 out of 30 indicates neurocognitive impairment.18

2) General practitioner assessment of cognition (GPCOG) test is of two parts

Patient examination

Informant interview

- If patient scores 0-4 out of 9, cognitive impairment is indicated, if score is 5-8 out of 9, proceed with section 2.
- Further in section 2 (informant interview) if patient score is 0-3 cognitive impairment is indicated.
- The sensitivity of the GPCOG is 85%, the specificity is 86%. It is a good tool to rule out cognitive impairment.[19] The performance on the GPCOG seems to be independent from one's cultural and linguistic background.

3) International HIV dementia scale (IHDS): Using the cut-off of $\leq$ 10, the sensitivity and specificity for HIV dementia with the IHDS are found to be 80% and 55-57% respectively.[20]

4) Montreal cognitive test (MoCA): This test is similar to IHDS scale and score less than 26/30 are abnormal. The sensitivity and specificity of the MoCA for detecting mild cognitive impairment has been estimated to be 90% and 87% respectively.[21]

Functional status of the patient was assessed by using following instruments

- Katz Index of Independence in Activities of Daily Living
- Instrumental activities of daily living scale (IADL).

a) The Katz Index of Independence in Activities of Daily Living, commonly referred to as the Katz ADL, is an appropriate instrument to assess functional status as a measurement of the client's ability to perform activities of daily living independently. Clinicians typically use the tool to detect problems in performing activities of daily living and to plan care accordingly. The Index ranks adequacy of performance in the six functions of bathing, dressing, toileting, transferring, continence, and feeding. Clients are scored yes/no for independence in each of the six functions. A score of 6 indicates full function, 4 indicate moderate impairment, and 2 or less indicates severe functional impairment.

b) Instrumental activities of daily living scale (IADL) The Instrumental Activities of Daily Living (IADL) Scale is used to assess independent living skills of an individual and measures functional ability as well as declines and improvements over time. The test measures eight realms of function through self-report, which attempt to assess everyday functional competence. Each domain measured by the scale relies on either cognitive or physical function, though all require some degree of both.

Scoring / Interpretation: The Lawton IADL scale can be scored in several ways, the most common method is to rate each item either dichotomously (0 = less able, 1 = more able) or trichotomously (1 = unable, 2 = needs assistance, 3 = independent) and sum the eight responses. The higher the score, the greater the person's abilities. Women are scored on all 8 areas of function, but, for men, the areas of food preparation, housekeeping, laundering are excluded. Clients are scored according to their highest level of functioning in that category.

A summary score ranges from 0 (low function, dependent) to 8 (high function, independent) for women, and 0 through 5 for men.

Abnormal score found in any of the mentioned neurocognitive tests was considered significant and patient was classified into asymptomatic neurocognitive impairment (ANI), HIV-associated mild neurocognitive disorder (MND) or HIV-associated dementia (HAD). The data was then processed using MS Excel and Epi info 7 and results were compared with similar studies done earlier in our country.

RESULTS

One-year prospective study beginning from July2012 to June 2013 was conducted in the department of Medicine in collaboration with department of Psychiatry and Neurology at IGMC, Shimla.105 HIV positive patients were screened for HAND, out of them 41 patients (39.04) were found to have HAND, 39 patients (95.1%) were having asymptomatic cognitive impairment, 2 patients (4.9%) were having mild cognitive impairment and 1 patient (2.08%) was having HIV associated dementia.

Demographic characteristics

Age distribution (Table 1): The age group of study population ranged from 30 years to 50 years. The mean age was 41.8 ± 5.9 years. Majority of the patients (n=27) were in the age group 40-50 years (65.8%). Fourteen patients were in the age group 30-40 years (34.2%). Mean age for females was 40.7 ± 6.2 years and for males was 42.5 ± 5.7 years.

Table 1: Age distribution.

Age group (years)	No. of patients (n)	%
30-40	14	34.2
40-50	27	65.8

Sex distribution (Table 2): Out of 41 patients included in the study, 25 (60.9%) were males and 16 (39%) were females. The male female ratio was 1.6:1.

Table 2: Sex distribution.

Sex	No. of patients (n)	%
Male	25	60.9
Female	16	39.1
Total	41	100

Marital status (Table 3)*:* All patients were married but 4 of them were widowed.

Table 3: Marital status of patients.

Sex	Total	Married (spouse alive)	Widowed
Male	25	24	1
Female	16	13	3

HIV status of spouses (Table 4): Spouses of 39 patients were HIV positive. HIV status of spouse of 2 patients was not known. Spouses of 24 males were HIV positive but status of spouse of 1male patient was not known. Spouses of 15 females were HIV positive, status of spouse of 1female patient was not known.

Table 4: HIV status of spouses.

Sex	Total	Spouse HIV positive	Spouse HIV status not known
Male	25	24	1
Female	16	15	1

Occupation of patients

Occupation of male patients (Table 5): Out of 25 male patients 18 were driver by occupation, 4 were factory workers, 2 were labourer and 1 was health worker. Out of 16 females one was peon and rest 15 were housewives.

Table 5: Profession of male patients.

Profession	No. of patients (n)	%
Driver	18	72
Factory worker	4	16
Labourer	2	8
Health worker	1	4

Occupation of female patients (Table 6): Out of 16 females 15 were housewives and 1 was peon at a school.

Table 6: Profession of female patients.

Profession	No. of patients (n)	%
Housewife	15	93.7
Other	1	6.3

Domicile: All patients in this study were from rural background.

Anthropometric / characteristics

Height, weight and BMI (Table 7): Mean height of patients in this study was 157.2 ± 6.6 cm. Mean weight was 54.9 ± 6.4 kg. Mean weight for males was 55.4 ± 4.7kg and for females was 54 ± 8.5 kg. Mean BMI for all patients was 22.3 ±2.6 kg/m2. Mean BMI for male patients was 22.7 ± 3.6kg/m2 and mean BMI for female patients was 21.9 ± 1.9 kg/m^2.

Table 7: Height, weight, and BMI of patients.

Variables	Overall (SD)	Male (SD)	Female (SD)
Mean Height(cm)	157.2 (6.6)	159(6.5)	154.4(5.6)
Mean Weight(kg)	54.8(6.4)	55.4 (4.7)	54 (8.5)
Mean BMI(kg/m^2)	22.3 (2.6)	22.7 (3.6)	21.9(1.9)

Illness characteristics

Route of transmission: All patients in our study gave history of heterosexual contact. None of them gave history of homosexual contact or intravenous drug abuse.

Average duration since detection of HIV: Average duration since diagnosis of HIV to detection of HAND was 3.7± 1.7 years. It ranged from 2.6 to 12 years. Average duration in males since detection of HIV was 3.7 ±1.4 years. Average duration in females since detection of HIV was 3.8 ± 1.6 years.

Treatment regimen and duration on current regimen: Out of 41 patients 12 patients were on SLN (stavudine, lamivudine, nevirapine) regimen (5 males, 7 females), 26 patients were on ZLN (zidovudine, lamivudine, nevirapine) regimen (17 males, 9 females), 1 patient on ZLE (stavudine, lamivudine, efavirenz) regimen (1 male) and 2 patients on SLE (stavudine, lamivudine, efavirenz) regimen (2 males). Mean duration of treatment was 17.2 months. Characteristics of patient depending upon treatment regimen (Table 8).

Table 8: Characteristics of patient depending upon treatment regimen.

	ZLN	SLN	SLE	ZLE
No. of patients	26	12	2	1
Male	17	5	2	1
Female	9	7	0	0
Mean age (yrs)	43.3	40.2	35.5	36
Mean duration since diagnosis of HIV(yrs)	3.9	3.3	2.7	5.4
Mean duration on present treatment(months)	16.4	18.3	18	24
Nadir CD4 count (per mm^3)	115.9	139.9	124.8	208
Mean BMI(kg/m^2)	21.8	23.1	22.1	25.6
Average hemoglobin (gm%)	11.2	10.9	10.3	13.2
Mean score IHDS	10.1	9.8	9	11
Mean score MMSE	19.7	20.8	21.5	23
Mean score MoCA	19.2	20.9	22.5	24

Age at presentation: Mean age at presentation was 43.3 years for patients on ZLN regimen, 40.2 years for patients on SLN regimen, 35.5 years for patients on SLE regimen, 36 years for patients on ZLE regimen.

Duration from diagnosis of HIV positive to detection of HAND: Mean duration from diagnosis of HIV positive to detection of HAND was 3.9 years for patients on ZLN regimen, 3.3 years for patients on SLN regimen, 2.7 years for patients on SLE regimen, 5.4 years for patients on ZLE regimen.

Nadir CD4 count: Mean nadir CD4 count was 115.9/mm3 for patients on ZLN regimen, 139.9/mm3 for patients on SLN regimen, 124.8/mm3 for patients on SLE regimen, 208/mm^3 for patients on ZLE regimen.

BMI (body mass index): Mean BMI was 21.8 kg/m2 for patients on ZLN regimen, 23.1 kg/m^2 for patients on SLN regimen, 22.1 kg/m2 for patients on SLE regimen, 25.6 kg/m^2 for patients on ZLE regimen.

Hemoglobin: Mean hemoglobin was 11.2 gm% for patients on ZLN regimen, 10.9 gm% for patients on SLN regimen, 10.3 gm% for patients on SLE regimen, 13.2 gm% for patients on ZLE regimen.

Score on dementia scales: Mean score on IHDS scale was 10.1 for patients on ZLN regimen, 9.8 for patients on SLN regimen, 9 for patients on SLE regimen, 11 for patients on ZLE regimen.

Mean score on MMSE scale was 19.7 for patients on ZLN regimen, 20.8 for patients on SLN regimen, 21.5 for patients on SLE regimen, 23 for patients on ZLE regimen. Mean score on MoCA scale was19.2 for patients on ZLN regimen, 20.9 for patients on SLN regimen, 22.5 for patients on SLE regimen, 24 for patients on ZLE regimen. Most of the patients were on ZLN and SLN regimen. On comparing the scores of patients on dementia scales on ZLN and SLN regimen, they were not statistically significant.

Laboratory parameters

Hemoglobin: Average hemoglobin was 11.1 gm% ± 1.0. Average hemoglobin was 11.3 ± 1.0 gm% for male patients and 10.8 ± 0.9 gm% for female patients.

CD4 count: Mean baseline CD4 count was 128.04/mm^3, minimum baseline CD4 count was 23/mm^3, maximum baseline CD4 count was 239/mm^3, mean baseline CD4 count was 118.6/mm^3 for males, mean baseline CD4 count for females was 142.9/mm^3. Mean nadir CD4 count was 126.1/mm^3, mean nadir CD4 count for males was 116.1/mm^3, mean nadir CD4 count for females was 141.9/mm^3. Scores on dementia scales (Table 8): Average score on montreal cognitive assessment scale was 20.8. Average score on MMSE was 20.5. Average score for international HIV dementia scale was 9.5.

Table 9: Scores on dementia scales.

Scale	Average score
IHDS	9.5
MoCA	20.9
MMSE	20.5

Characteristics of patients divided into two groups according to CD4 count (Table 10): These 41 patients detected to have HAND were further stratified according to CD4 count. Since number of patients having nadir

CD4 count more than 200 were very less in this study. So, patients were divided into two groups: one with nadir CD4 count more than 150/mm3 and other with nadir CD4 count less than 150/mm^3.

Table 10: Characteristics of patients divided into two groups according to CD4.

	CD4>150	CD4<150
No. of patients	13	28
Male	6	19
Female	7	9
Mean age(yrs)	38.61	50
Mean duration since diagnosis of HIV(yrs)	3.61	4.1
Mean height(cm)	154.9	158.2
Mean weight(kg)	54.7	54.9
Mean BMI(kg/m^2)	22.9	21.9
Average hemoglobin(gm%)	11.2	11.1
Mean score IHDS	10.1	9.6
Mean score MMSE	21.5	20.4
Mean score MoCA	21	19.8

There were 13 patients having nadir CD4 count more than 150 out of them 6 were male and 7 were female. 28 patients were having CD4 count less than 150, 19 were males and 9 were females.

Age of presentation: Mean age of presentation was 38.6 years in patients having nadir CD4 count more than 150 and 50 years in patients with nadir CD4 count less than 150. Duration from diagnosis of HIV to detection of HAND: Mean duration from diagnosis of HIV to detection of HAND was 3.6 years in patients with nadir CD4 count more than 150 and 4.1 years in patients with nadir CD4 count less than 150.

BMI (body mass index): Mean BMI was 22.9 Kg/m2 in patients with nadir CD4 count more than 150 and 21.9 kg/m2 in patients with nadir CD4 count less than 150.

Hemoglobin: Average hemoglobin was 11.2gm% in patients of nadir CD4 count more than 150 and 11.1gm% in patients with nadir CD4 count less than 150.

Score on dementia scales: Mean score on IHDS scale was 10.1 in patients with nadir CD4 count more than 150 while it was 9.6 in patients with nadir CD4 count less than 150 ($p<0.05$). Mean score on MMSE scale was 21.5 in patients with nadir CD4 count more than 150 while it was 20.4 in patients with nadir CD4 count less than 150.Mean score on MoCA scale was 21in patients with nadir CD4 count more than 150 while it was 19.8 in patients with CD4 count less than 150 ($p<0.05$).

DISCUSSION

HIV/AIDS affects all body systems including central nervous system. People with HIV commonly experience at least minor signs of thinking and memory problems. Many problems are so minor, however, that people don't realize that they have any dysfunction. The present study was designed to know such neurocognitive dysfunction in HIV patients in this part of country.

In the present study age of the patients ranged from 30 - 50 yrs and the mean age was 41.83 years. McCombe JA et al from Canada found that the mean age of patients having HIV associated neurocognitive disorders was 43.8 years.[22] A study by Vijay D. et al from India including 1606 HIV patients found median age of 36 years in patients with neurologic manifestations.[10] Mean age of presentation of our patients is almost similar to that of these studies.

Average duration from diagnosis of HIV to detection of HAND was 3.77 years in this study. McCombe JA. et al noted duration since detection of HIV to detection of 11.8 yrs but they also noted that duration since diagnosis of HIV didn't predicted HAND.[22] Average duration since detection of HIV to diagnosis of HAND may be lower in our study due to simultaneous presence of comorbidities like anemia, malnutrition which can affect cognition.

Keeping in view the profession (driving, army), travelling and sexual behavior in a male dominant society there is male predominance in majority of the studies. Chan LG. et al in South Asian population reported 86% male patients.[23] Whereas a study from Canada noted 80% male patients.[24] In our study, also males dominate the sample (60.9%) males. People in certain profession have been found to be more susceptible to contract HIV. In a study conducted by Vishwanath B.M. et al drivers and businessman constituted 77.4% of all HIV positive patients.[25] Drivers accounted for 72% of the total HIV male patients in our study. The nature of work in these professions forcing them to stay away from homes could be attributed for their greater susceptibility to high risk behavior and thus to acquire HIV infection. Most of females in our study were housewives. This observation is comparable to study done by Adhikari et al.[26]

Unprotected multiple heterosexual contacts with professional sex workers has been demonstrated as the predominant mode of HIV transmission accounting for 70-96% of all cases in several studies. This large variation can be explained on the basis of variation in rural versus urban distribution of population, prevalence of intravenous drug abuse, availability of red light areas or commercial sex workers in different parts of the world. In our study heterosexual contact was the commonest mode of transmission of HIV. All 25 (60.9%) male patients had multiple unprotected sexual exposures. The husbands of all females in present study were HIV positive. In a study conducted by Sircar AR et al heterosexual mode of transmission occurred in 82% subjects and in another study by Adhikari et al this mode was responsible for 83% of HIV transmissions.[27,26] The finding in our study in this respect is comparable with

these studies. As far as marital status is concerned all subjects were married in the present study. Majority of the patients (85.92%) were also married in a study done by Vishwanath BM. et al which is comparable to our finding.[25]

Relation between BMI and neurocognitive dysfunction in HIV patients has been investigated in several studies. Dolan et al from Boston observed that mean BMI was 22.1kg/m^2 in male patients having neurocognitive dysfunction and 20.8 kg/m^2 in females.[28] Mean BMI of all patients was 22.3 kg/m^2 in our study. Considering separately, it was 22.7 kg/m^2 for male and 21.9 kg/m^2 for female patients respectively. The values are similar to above study. Patients having CD4 count less than 150 were having lower mean BMI 21.9 kg/m^2 in our study.

HIV associated neurocognitive dysfunction (HAND) has been shown to be associated with low nadir CD4 counts in the absence of central nervous system opportunistic infections. Various studies are conducted across the world to see the relationship between CD4 count and HAND. Mean baseline CD4 count was 128.04/mm^3 in our study and nadir CD4 count was 126.1/mm^3. Patients of HAND with nadir CD4 count less than 150 were having mean age of 50 years in our study and mean duration since HIV positive was 4.1 years in our study. Vijay D. Teja et al observed median CD4 count of 89/mm^3 in an Indian hospital based study on 123 patients with neurologic manifestations.[10] Study by McCombe JA.et al also observed mean nadir CD4 count of 101.4/mm^3.[22] Chan L.G. at al in their study observed that the patients with HAND tend to be older (mean 54.4 years), with fewer years of formal education (mean 8.0), and had extremely low baseline CD4 counts (CD4 <200 cells/µl).[23] Our study is consistent with the finding of these studies in this respect.

Patients of HAND perform poorly in the domains of delayed recall, language, abstract thinking, motor speed and psychomotor speed.[23] In our study, average score on MMSE was 20.5, average score on MoCA was 20.8 and IHDS was 9.5. Chan L.G. et al[23] observed an average MoCA score 24.2, average IHDS score 8.6 in their study. In a South Indian study Reidel D. et al also observed that 35% of patients had IHDS score less than 10.[29] In our study 39.04% patients had HAND and out of which 4.87% patients had mild cognitive impairment, 2.08% had HIV associated dementia and rest had asymptomatic neurocognitive impairment. Gupta J.D. et al[7] on South Indian patients noted 60.5% had mild to moderate cognitive deficits while no subject had severe cognitive deficit. Wig N. et al from New Delhi observed that 42% of subjects had HIV associated mild neurocognitive disorder and 1.02% had HIV associated dementia.[30] Our study is consistent with these two studies.

Standard treatment for HIV-associated dementia includes potent antiretroviral therapy but some studies also suggested that cART may lead to HAND. Antiretroviral regimens with good CNS penetration such as nevirapine, efavirenz were associated with poorer neurocognitive performance according to Marra et al.[31] While Cross S et al observed that cART preserves or improves cognition in HIV infected patients after 1 year, irrespective of the regimen's CPE.[32] In our study average duration on cART was 17.2 months. Majority of patients (n=26, 63.3%) having HAND were on ZLN (zidovudine, lamivudine, nevirapine). Patients on ZLN regimen scored less on dementia scales as compared to those on other regimens but it was not statistically significant. Our study was not sufficiently large to comment on this issue and duration of treatment was also not sufficiently long.

CONCLUSION

The conclusion of the study is that HIV associated neurocognitive disorder is common and asymptomatic neurocognitive impairement is the commonest type of HIV associated neurocognitive disorder in HIV positive patients. It can be detected while patient is asymptomatic with help of simple neurocognitive tests. Although few studies reported higher prevalence of HIV associated neurocognitive disorder among patients on certain combined antiretroviral therapy (cART) regimen but our study didn't indicate any such association. Further, it is also concluded that a simple neurocognitive test can identify HIV associated neurocognitive dysfunction (HAND) even though the patient is asymptomatic so that appropriate management strategies can be instituted to improve the survival and quality of life in HIV infected patients. Thus, every HIV patients should be screened for HIV associated neurocognitive disorder whenever possible.

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