Section: Medicine

Original Research Article

STUDY OF NEUROCOGNITIVE DYSFUNCTION IN HIV INFECTED PATIENTS AND ITS CORRELATION WITH CD4 COUNT

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Abstract

Background: HIV infected individuals demonstrate a high prevalence of neurocognitive deficits. While CD4 count remains a valuable prognostic marker for HIV disease progression, a comprehensive understanding of the underlying mechanism of neurocognitive decline including role of immune activation and CD4 count is yet to optimized. Study of neurocognitive dysfunction in HIV infected patients and its correlation with CD4 count. **Materials and Methods:** International HIV dementia scale (IHDS) and Katz Index of Independence in Activities of Daily Living were used for diagnosing neurocognitive dysfunction in a total of 143 HIV infected patients. Data was analysed using STATA statistical software version 16.0 and P- value of less than 0.05 was taken as statistically significant. **Result:** Among 143 participants, 69 PLHIV (47.26%) had HIV associated neurocognitive disorder. In the patients having neurocognitive dysfunction, 43.15% belonged to Stage 1 category. The association between WHO clinical stage, based on CD4 count, and the HIV Associated Neurocognitive Disorder were found to be statistically significant (p-value: 0.013). **Conclusion:** Cognitive decline at any stage of life can be accelerated by HIV infection which can affect ability of PLHIV to lead an independent and quality life.

INTRODUCTION

HIV - associated neurocognitive disorders (HAND) are defined as impairment of multiple cognitive domains in association with HIV in the absence of other causes for the impairment.[1] 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 primarily due to the pathogenic processes of HIV infection or secondarily due to opportunistic infections or neoplasms. Among the more frequent opportunistic disease that involves the CNS are toxoplasmosis, cryptococcosis, progressive multifocal leukoencephalopathy, and primary CNS lymphoma. Other less common problems include mycobacterial infection, syphilis, infection with CMV, herpes zoster, HTLV-1, Trypanosoma cruzi, or Acanthamoeba. Overall, secondary disease of the CNS has been reported to occur in approximately one- third of the patients with AIDS. These antedates the widespread use of combined antiretroviral therapy (cART), and this frequency is considerably lower in patients receiving effective antiretroviral drugs.[2] Since the introduction of combined antiretroviral therapy (cART) in 1996, the HIV 1 infection has become a treatable condition.[3] However, HIV infection is an incurable disease as several attempts to eradicate the virus have so far been unsuccessful. The cerebral manifestations of HIV infection with disturbance of cognitive, behavioural, motor and autonomous functions remain an issue in everyday practice of HIV medicine. The current terminology of HAND is based on a 2007 revision of older classification of 1991 and was triggered by the fact that the disease course was considerably altered by combined antiretroviral therapy (cART). The current terminology of neurocognitive impairment (NCI) comprises the

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category of asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and HIV associated dementia 4.Neuropathological, neuropsychological and in-vivo imaging studies have generated evidence of persistent HIV – associated neurodegenerative processes and HAND despite successful HAART, though its onset appears to be delayed and severity reduced, while HIV patients live longer with HIV infection. Long term HIV infection may facilitate the development of other neurodegenerative diseases and accelerate aging processes. The pathogenic mechanism underlying HAD involved neurotoxicity and impaired neurogenesis and seems to heavily depend on the overall condition of immune system. Although immune suppression and lack of lymphocytes apparently favor cognitive impairment, infected and activated macrophages and microglia seem to be major factor promoting the development of HAD 5.Unlike other states of India, HIV transmission in Manipur is mainly correlated with the sharing of HIV-infected injecting equipment/needles among the IDUs. IDUs are the easy prey for contracting HIV. Although the epidemic was initially described among IDUs, HIV is no longer confined to IDUs but it began to appear in the general public. Manipur, a far north-eastern corner of the country with hardly 0.2% of country's population is contributing nearly 8% of India's total HIV-positive cases 6. Thus, the present study was undertaken to study the neurocognitive dysfunctions in HIV infected patients attending RIMS, Imphal, Manipur. Furthermore, the relation between HIV associated neurocognitive disorders and CD4 counts level.

MATERIALS AND METHODS

A cross sectional study was conducted at the Department of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur from January 2021 to October 2023 among HIV positive patients between 18 to 60 years of age admitted in Medicine ward, attending Medicine OPD and CoE ART Centre, RIMS, Imphal. Patient with history of psychiatric illness, stroke, meningitis, head injury and epilepsy were excluded from the study.A sample size of 143 was calculated using the formula N = 4PQ/ L2, where Prevalence of HIV associated neurocognitive disorder (HAND) data was taken from Achappa et al 7 which was 90.1%. Convenience sampling was done. Age, sex, education, marital status, ART drug history, HIV viral load, etc. were the independent variables and International HIV dementia scale (IHDS), Katz Index of Independence in Activities of Daily Living, CD4 count were the dependent variables.

Working definition:

According to Frascati criteria 2, HIV associated neurocognitive disorders (HAND) was classified in three categories: Asymptomatic neurocognitive impairment (ANI): Abnormality in two or more cognitive abilities with no functional impairment, Mild neurocognitive disorder (MND): Cognitive impairment with mild functional impairment and HIV- associated dementia (HAD): Marked cognitive impairment with marked functional impairment.

International HIV dementia scale (IHDS) 8: The IHDS consists of three subsets: timed finger tapping, timed alternate hand sequence test, and recall of four items in two minutes.

Interpretation: A total score, out of 12 was calculated for each participant with each subset contributing 4 points to total score. The maximum possible score was 12 points. A patient with a score of ≤ 10 was further evaluated for possible dementia.

The Katz Index of Independence in Activities of Daily Living 9:

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 plan care accordingly.

Interpretation: Patients' responses were recorded as either "yes" or "no" for ability to do an activity independently or not, in each of the six functions. For conducting each of the activities independently, patients were scored one (1). On the other hand, if the patient had to manage the same activity under supervision/direction/personal assistance or that particular activity was done by someone else completely, in such condition, that individual was scored zero (0) point. In this manner if a patient was able to handle all the six activities on his/her own, he/she was provided the highest score of six (6) and the lowest score was zero (0), for those who were unable to perform any of the six activities on his/her own at all. As per the scoring criteria, a score of 6 indicates full function, 4 indicates moderate impairment, and 2 or less indicates severe functional impairment.

Data collection procedure:

The study was carried out with the clearance from the Research Ethics Board [reference no. A/206/REB-Comm(SP)/RIMS/2015/760/102/2020]. Informed written consent was taken from the patient. All the selected patients were subjected to comprehensive questionnaire for neurocognitive disorders by International HIV dementia scale (IHDS), and Katz index for functional status of patient, history taking and thorough detailed examination. All the routine examination was done as per NACO recommendation. Blood samples were sent for CD4 count. All the data collected was documented, analyzed statistically to draw a useful conclusion and assessed for any neurocognitive disorders. A total confidentiality of patient's data was maintained throughout the study.

The collected data were entered in Microsoft Excel and analyzed by using STATA statistical software version 16.0 for Windows (Stata Corp, College Station, TX, US). Summarizations of data were carried out by using descriptive statistics such as

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mean, standard deviation and percentages. Chi-square test and Fisher's exact test were employed to test the association between two proportions of outcome variables and variables of interest like sex, age, marital status, etc. The p-value of less than 0.05 was taken as statistically significant.

RESULTS

During the study period, a total of 146 HIV positive participants were enrolled. All of them were adults and their age varied between 18 years to 60 years at the time of interview [Table 1]. Their average age was calculated as 44.79 years with a standard deviation (SD) of 11.14 years. Median age of the participants was found to be 46 years with an inter-quartile range (IQR) of 15 years (IQR: 38 to 53 years). Among the participants 62.3% were male as shown in table 1. Twenty patients (13.70%) never received any formal education and forty four patients (30.14%) were unemployed as shown in table 1. Majority [87 (59.59%)] of the patients were reported to be married.

In [Table 2], HIV positive patients were suffering from HIV for a varied period of time, from newly diagnosed to as long as 20 years. Their mean and median years of diagnosis were 9.75 and 10 years with a standard deviation of 5.51 years and IQR of 5 to 10 years, respectively. When participants were enquired about the route of transmission of the HIV, several routes came into their responses. Majority of the participants mentioned of heterosexuality [85, 58.22%] as the route of infection, followed by use of intravenous drugs through shared needles [38, 26.03%], blood transfusion [3, 2.05%] and a few other ways [6, 4.11%]. Another very important route of transmission, from infected mother to the child, i.e., perinatal transmission was also found in significant number of patients [14 (9.59%]. Forty three patients (30.07%) were, in one way or another, involved in some kind of high-risk behavior. When asked about the spouse's HIV status, 64 of them reported that their spouses were diagnosed HIV positive too and 14 of them confirmed negative report; though another 37 individuals could not confirm the HIV status of their spouses.

Participants' blood report was collected for evaluating several blood parameters, CD4 count was one of them, which is used to identify the severity of the HIV infection. Participants' mean CD4 count was calculated to be 511.45 with a standard deviation of 515.93, ranging between as low as 10 and 5922 at the highest point. The median CD4 count was found to be 442, with a count of 25th percentile and 75th percentile at 311 and 620, respectively as shown in [Table 3]. As per the WHO clinical staging, the CD4 count was further classified into four groups, named as Stage 1(500cells/µl), where the patients remain asymptomatic, Stage 2(350-499cells/µl), where the patient develops mild symptoms, Stage 3 (200-349cells/µl), where the patient develops advanced symptoms and finally the severe symptoms arrive at the Stage 4 (<200cells/µl). Among the participants, the greater section [63, 43.15%] belonged to the Stage 1 category. Mild symptoms were developed among 39 (26.71%) of the samples. Further, 25 (17.12%) patients developed advanced symptoms, belonging to the Stage 3 category. And lastly, 19 (13.01%) of them were found to be exhibiting Stage 4 symptoms as displayed in [Table 3].

[Table 4] shows more than half of the participants [73, 51.05%] mentioned that they were suffering from hypertension. Little more than one-fourth of the participants [37, 26.06%] reported to be suffering from tuberculosis followed by diabetes, which affected nearly one-fifth of the participants [29, 20.28%]. Hepatitis C virus infection was more common among the participants, than the hepatitis B infection [Hepatitis B: 1 (0.82%) and Hepatitis C: 8 (6.45%)].

Mean haemoglobin value was found to be 12.94 ± 10.69 grams/dl, ranging between 0.2 and 134 grams/dl as shown in table 5. Most of the participants were anaemic [100, 68.49%] followed by individuals with normal haemoglobin level [41, 28.08%]. Participants' random blood sugar (RBS) level ranged between 67 mg/dl and 402 mg/dl with a mean RBS value of 127.01 ± 47.51 mg/dl. Serum creatinine of the respondents varied between 0.37 and 12.5 mg/dl. Serum creatinine level was within normal range for the majority 127 (86.99%), and higher among 18 (12.33%) patients. Blood sample from only one (0.68%) patient was found to be lower than normal serum creatinine level. Besides these, SGOT values ranged between 8 unit/lt to maximum of 715 unit/lt of serum. Mean value of SGOT was found to be 62.90 units/liter of serum, which was quite higher than the normal range of 5 to 40 units/liter of serum. Among the participants, 64 (43.84%) recorded high SGOT and the rest [82, 56.16%] exhibited within normal range of SGOT. SGPT values ranged between 10 unit/lt to a maximum of 519 unit/lt of serum. Mean value of SGPT was found to be 61.53 units/lt of serum, which was at the higher side than the normal range. Among the participants, 41 (28.08%) recorded high SGOT and the rest [105, 71.92%] exhibited within normal range of SGOT. Mean value of ALP was found to be 208.17 ± 147.97 IU/lt, which was also at the higher side from the normal range. Values of ALP ranged between 17 IU/lt to maximum of 1110 unit/lt of serum. The median ALP value was 178 IU/lt followed by an IQR of 151 IU/dl (112-263 IU/dl). Among the participants, more than half of them [79, 54.11%] recorded high ALP level followed by 2.74% (4 out of 146 participants) with low ALP level and the rest [63, 43.15%] exhibited within normal range of ALP level.

[Table 6] shows the main outcome of this study, HIV Associated Neurocognitive Disorder (HAND), was based on two of the measuring tools, Katz Index of Independence in Activities of Daily Living and International HIV dementia scale (IHDS). The scores from the Katz Index of Independence in Activities of

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Daily Living were categorized into three groups, where 139 (95.21%) of the participants were found to be able to accomplish all the six activities on their own, so were classified as fully functional. Moderate functional impairment was observed in 4 (2.74%) of the individuals and severe form of functional impairment was presented by 3 (2.05%) of the participants. The second tool, International HIV dementia scale (IHDS) identified 67 (45.89%) individuals who required further assessment for dementia. The remaining 79 (54.11%) patients scored more than 10 out of 12, so, they did not require further assessment for dementia. Thus as shown in table 6 a little more than half of the participants [77, 52.74%], assessed, did not have HIV Associated Neurocognitive Disorder (HAND). 69 (47.26 %) People living with HIV had HAND. Among which, 63 (43.15%) of the participants were found to be affected of asymptomatic neurocognitive impairment (ANI), 4 (2.74%) of them were diagnosed with mild neurocognitive disorder (MND) and the remaining 2 (1.37%) patients had HIV- associated dementia (HAD).

[Table 7] shows among the 63 clinical Stage 1 patients, 35 (55.56%) scored >10 in the International HIV dementia scale, that means they didn't have dementia. Though the highest proportion of clinical Stage 4 patients [11 (57.89%)] exhibited that they didn't have dementia. Similar result was found in the group of Stage 2 [53.85%] also. Only in the Stage 3 cases, the proportion of dementia [13, 52.00%] was higher than the non-dementia cases, that was endorsed from the International HIV dementia scale. The association between WHO clinical stage, based on CD4 count, and the scored categories from International HIV dementia scale were found to be statistically insignificant (p-value: 0.91).

[Table 8] shows among the 63 clinical Stage 1 patients, 62 (98.41%) were identified as fully functional in the Katz Index of Independence in Activities of Daily Living and one (1.59%) were severely impaired to daily activities [Table 12]. All of the Stage 2 patients were identified as fully functional. All but just one (4.00%) were identified as moderately impaired among the clinical Stage 3 and the rest 24 (96.00%) were capable of accomplishing all the activities on their own. The proportion of impairment was higher among the clinical Stage 4 patients. 15.79% (3 out of 19) of the patients were moderately impaired and another 10.53% (2 out of 19) were detected as severely impaired, functionally. The association between clinical staging, based on CD4 count, and the Katz Index of Independence in Activities of Daily Living were found to be statistically significant (p-value: 0.001).

[Table 9] shows, 77 (52.74%) did not have HIV associated neurocognitive disorder. Among the clinical Stage 1 patients, 28 (44.44%) had asymptomatic neurocognitive impairment, and 1 (1.59%) had HIV-associated dementia. The clinical Stage 2 patients were having either asymptomatic neurocognitive impairment [18, 46.15%] or no neurocognitive disorder [21, 53.85%] were exhibited. Among the 25 Stage 3 patients, 13 (52.00%) were grouped under asymptomatic neurocognitive impairment and one (4.00%) were detected with mild neurocognitive impairment. Among the Stage 4 cases, 4 (21.05%), 3 (15.79%) and 1 (5.26%) were identified as asymptomatic neurocognitive impairment, mild neurocognitive disorder and HIV-associated dementia, respectively. The association between WHO clinical stage, based on CD4 count, and the HIV Associated Neurocognitive Disorder were found to be statistically significant (p-value: 0.013).

Table 1: Age and Sex of the study participants (N=146).

Age of the participants	
Mean (±SD)	44.79 (±11.14) years
Median (IQR)	46 (38-53) years
Range	18 - 60 years
Sex of the participants	
Male	91 (62.33%)
Female	55 (37.67%)
Educational Qualification	
No formal education	20 (13.70%)
Primary education	44 (30.14%)
Secondary education	60 (41.10%)
Graduate	22 (15.07%)
Occupations	
Shopkeeper	58, 39.73%
Unemployed	44, 30.14%
Government servants	21, 14.38%
Carpenter	2, 1.37%
Others	21, 14.38%
Marrital status	
Married	87 (59.59%)
Separated	10 (6.85%)
Widow	19 (13.01%)
Unmarried	30 (20.55%)

*SD: Standard Deviation; IQR: Inter-Quartile Range

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Table 2: HIV Profile of the study participants (N=146)

Years since diagnosed (n=146)	
Mean (±SD)	9.75 (± 5.51) years
Median (IQR)	10 (5-15) years
Range	0 – 20 years
Route of transmission (n=146)	
Perinatal transmission	14 (9.59%)
IVD	38 (26.03%)
Heterosexual	85 (58.22%)
Blood transfusion	3 (2.05%)
Others	6 (4.11%)
High risk behaviour	
Yes	43 (30.07%)
No	100 (69.93%)
HIV Status of the spouse (n=145)	
Positive	64 (44.14%)
Negative	14 (9.66%)
Not Known	37 (25.52%)
Not applicable	30 (20.69%)

*SD: Standard Deviation; IQR: Inter-Quartile Range

Table 3: Participants CD4 count and WHO clinical staging, based on CD4 count (N=146)

CD4 Count	
Mean (±SD)	511.45 (±515.93)
Median (IQR)	442 (311-620)
Range	10 - 5922
CD4 Count (cells/µl) (WHO Clinical Stage)	
Stage 1 (>500) (Asymptomatic)	63 (43.15%)
Stage 2 (350-499) (Mild symptoms)	39 (26.71%)
Stage 3 (200-349) (Advanced symptoms)	25 (17.12%)
Stage 4 (<200) (Severe symptoms)	19 (13.01%)

*SD: Standard Deviation; IQR: Inter-Quartile Range

Table 4: Disease profile of the study participants (N=146)

Diseases	**Present**	**Absent**
Hypertension	73 (51.05%)	70 (48.95%)
Diabetes	29 (20.28%)	114 (79.72%)
Tuberculosis	37 (26.06%)	105 (73.94%)
Hepatitis B Virus	3 (2.46 %)	119 (97.54%)
Hepatitis C Virus	10 (8.06%)	114 (91.94%)

Table 5: Blood parameters and liver function test of the study participants (N=146)

Blood Parameters	**Mean (±SD)**	**Median (IQR)**	**Range**
Haemoglobin	12.94 (±10.69)	11.9 (10.2-13.3)	0.2-134
Low	100 (68.49%)		
Normal	41 (28.08%)		
Higher than normal range	5 (3.42%)		
Random Blood Sugar	127.01 (±47.51)	113.5 (98-140)	67-402
Low blood sugar level	1 (0.68%)		
Normal blood sugar level	109 (74.66%)		
Prediabetic	26 (17.81%)		
Diabetic	10 (6.85%)		
Serum creatinine	1.12 (±1.27)	0.9 (0.8-1.0)	0.37-12.5
Low	1 (0.68%)		
Normal	127 (86.99%)		
High	18 (12.33%)		
Serum Glutamic-oxalate transaminase (SGOT) (u/lt)	62.90 (±87.96)	36.5 (27-56)	8-715
Normal	82 (56.16%)		
High	64 (43.84%)		
Serum Glutamic Pyruvic Transaminase (SGPT) (u/lt)	61.53 (±70.70)	42.5 (29-60)	10-519
Normal	105 (71.92%)		
High	41 (28.08%)		
Alkaline Phosphatase (ALP) (IU/dl)	208.17 (±147.97)	178 (112-263)	17 – 1110
Low	4 (2.74%)		
Normal	63 (43.15%)		
High	79 (54.11%)		

*SD: Standard Deviation; IQR: Inter-Quartile Range

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Table 6. Katz Index of Independence in Activities of Daily Living, IHDS score and HAND among the study populations (N=146)

Scales of measurement	Frequency (n, %)
Katz Index of Independence in Activities of Daily Living	
Fully functional	139 (95.21%)
Moderate functional impairment	4 (2.74%)
Severe functional impairment	3 (2.05%)
International HIV dementia scale (IHDS) score	
Less than or equal to 10	67 (45.89%)
More than 10	79 (54.11%)
HIV Associated Neurocognitive Disorder	
None	77 (52.74%)
Asymptomatic neurocognitive impairment (ANI)	63 (43.15%)
Mild neurocognitive disorder (MND)	4 (2.74%)
HIV- associated dementia (HAD)	2 (1.37%)

Table 7: Association of International HIV dementia scale score with CD4 count (N=146)

CD4 Count categories	Score from International HIV dementia scale		Pearson Chi-squared value	p-value
	Scored ≤10	Scored >10		
Stage 1	28 (44.44%)	35 (55.56%)	0.5396	0.91
Stage 2	18 (46.15%)	21 (53.85%)		
Stage 3	13 (52.00%)	12 (48.00%)		
Stage 4	8 (42.11%)	11 (57.89%)		
Total	67 (45.89%)	79 (54.11%)		

Table 8: Association of Katz Index of Independence in Activities of Daily Living and CD4 count (N=146)

CD4 Count categories	Katz Index of Independence in Activities of Daily Living			Pearson Chi-squared value	p-value
	Fully functional	Moderate functional impairment	Severe functional impairment		
Stage 1	62 (98.41%)	0 (0.00%)	1 (1.59%)	23.8558	0.001
Stage 2	39 (100.00%)	0 (0.00%)	0 (0.00%)		
Stage 3	24 (96.00%)	1 (4.00%)	0 (0.00%)		
Stage 4	14 (73.68%)	3 (15.79%)	2 (10.53%)		
Total	139 (95.21%)	4 (2.74%)	3 (2.05%)		

Table 9: Association of HIV Associated Neurocognitive Disorder and CD4 count (N=146)

CD4 Count categories	HIV Associated Neurocognitive Disorder				Pearson Chi-squared value	p-value
	None	Asymptomatic neurocognitive impairment	Mild neurocognitive disorder	HIV-associated dementia		
Stage 1	34 (54.97%)	28 (44.44%)	0 (0.00%)	1 (1.59%)	20.9450	0.013
Stage 2	21 (53.85%)	18 (46.15%)	0 (0.00%)	0 (0.00%)		
Stage 3	11 (44.00%)	13 (52.00%)	1 (4.00%)	0 (0.00%)		
Stage 4	11 (57.89%)	4 (21.05%)	3 (15.79%)	1 (5.26%)		
Total	77 (52.74%)	63(43.15%)	4(2.74%)	2 (1.37%)		

DISCUSSION

All the participants of this study were HIV positive patients attending CoE ART center and inpatients from the Department of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur. Average age of the participants was 45 years. Number of male participants was close to double of female. On average, these patients were living with HIV infection for 10 years. Around 60% of them mentioned sexual transmission as the route of infection, and the second most common route was intravenous drug use by shared needle. Among the spouses of HIV positive patients around 56% of them were found to be HIV positive too. Average CD4 count of the participants were 511.45 cells/µl and this ranged between 10 to 5922 cells/µl. Though most of them were asymptomatic or having mild symptoms, more than 30% of the participants' CD4 count was less than 350 cells/µl; 13% of the participants had a CD4 count below 200 cells/µl.

Hemoglobin level was low for the majority. Blood parameters of liver function test showed, SGOT level was higher than normal for almost half of the patients, more than one-fourth of the participants had elevated serum SGPT. Alkaline phosphatase (ALP) level was on the higher side for more than half of the patients. ALP level was low for around 3% of the participants too. Besides HIV infection, participants were found to be affected with other diseases, such as hypertension, diabetes, tuberculosis, and hepatitis B and hepatitis C, which is common in HIV infected patients.

Through the Katz Index of Independence in Activities of Daily Living tool, only 7 of the participants, those counted for nearly 5% of the study population, were found to be functionally impaired. However, while tested through the International HIV dementia scale (IHDS), around 46% of the participants were found to be suffering from some level of dementia. HIV Associated Neurocognitive Disorder was found among 47.26 % of the study

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population. Among them, two of the patients were diagnosed as suffering from HIV-associated dementia (HAD). In the rest, only 2.74% patients had mild neurocognitive disorder (MND) and asymptomatic neurocognitive impairment (ANI) was found in 43.15% of them. The association with CD4 count was statistically significant for Katz Index of Independence in Activities of Daily Living and HIV associated neurocognitive disorders (HAND), but was not significant with International HIV dementia scale (IHDS).

In this study the average CD4 count was found to be 511 cells/µl and there were nearly 57% of the study population, whose CD4 count were below 500 cells/µl and 13% of the populations' CD4 count was below 200 cells/µl. A study from Shimla, Himachal Pradesh, a northern Indian state, reported CD4 count, less than 150 cells/µl among 68.3% of the 41 study samples with HIV Associated Neurocognitive Disorder 10. This difference in prevalence is probably due to smaller sample size, that was restricted to patients with HIV Associated Neurocognitive Disorder only. Another study from tertiary care hospital of Tripura, a north-eastern state of India, conducted on 261 HIV positive patients. They reported a range of 150-249 cells/µl CD4 count in case of 62.5% of the participants, which was quite on the higher side than this study.[11] The possible reasons could be due to difference in HIV prevalence between the two states,[12] behavioural differences, geographic location and related social unrest etc.[13]

The levels of liver function test parameters, i.e. level of aspartate aminotransferase (AST, also known as SGOT), alanine aminotransferase (ALT, also known as SGPT) and alkaline phosphatase (ALP) were measure for all the participants, where we observed any one or other was elevated for most of the participants. The mean values of SGOT and SGPT levels from our study population were 62.90 ± 87.96 and 61.53 ± 70.70 respectively. These findings were found similar to another study on caucasian population where the researchers found the mean ALT value of 62.6 u/lt among HIV patients with HCV co-infection, though the mean value of AST (42.7 u/lt) was lower than the results of this study.[14] Among Thai individuals with HIV a study was conducted by Peluso et al,[15] where the authors have mentioned and discussed about elevated ALT levels which is common in acute HIV infection, that supports our study finding of elevated ALT level of more than half of our study populations.

HAND was found among 47.26 % of the study population, and asymptomatic neurocognitive impairment (ANI) covered most of them. Heaton et al., in a study on 1,555 HIV infected American adults with diverse characteristics found that 52% of the total sample had neuropsychological impairment,[16] that backed our study finding. They also reported 33% for ANI, 12% for MND and only 2% for HAD, which means ANI with highest prevalence, followed by MND and HAD. Though the prevalence varies from our findings, except for HAD, the sequence was maintained in our population. Muniyandi et al,[17] conducted a similar assessment where the authors discussed that asymptomatic cognitive impairment was very common in AIDS patients; however, the prevalence of ANI was nearly 91% (63 of 69 patients with HAND) in our study which was notable higher than the other study, where ANI was reported at 69% (23 of 33 patients). But the prevalence in the other two categories of HAND, i.e., MND and HAD, were 5.8% and 2.9% respectively which were in harmony with this study. With contrast to our findings, Achappa et al,[7] reported from Mangalore that 90.1% of the patients had HAND, which was significantly higher. Heaton et al., in a study on 1,555 HIV infected American adults with diverse characteristics found that 52% of the total sample had neuropsychological impairment.[16]

The criteria of categorizing HAND were based on Frascati Criteria.[1] HAND was found to be significantly associated with CD4 count (p-value: 0.013) in this study. Muniyandi et al,[18] mentioned, as the CD4 count reduces, the chance of having HIV dementia increases significantly supporting the same theory.

American Academy of Neurology Task Force on AIDS describes two neurobehavioral disorders in HIV.[18]

1. HIV-Associated Minor Cognitive Motor Disorder (MCMD) and
2. HIV-Associated Dementia Complex (HADC)

In MCMD, the psychological defects are mild and cause only mild functional impairment. In HADC, defects are moderate to severe and interfere with day-to-day living. The HIV enters the brain shortly after infection and has a predilection for subcortical brain areas.[19,20] The cognitive impairment is attributed to HIV replication in brain and liberation of inflammatory neurotoxins leading to impairment of natural host repair mechanisms. This leads to neuronal dysfunction, injury, or death.[21]

Dementia in AIDS indicates an increased risk of mortality.[22-24] The presence of dementia interferes with ART treatment, which is the bed rock of AIDS management. ART could improve cognitive function with poor physical condition and immune status, but it does not considerably improve.[25,26] Hence, it is imperative that cognitive impairment should be recognized early in a HIV positive patient to enhance drug compliance to ART.

Of recent interest is that of research detailing the potential efficacy of neurofilament light chain proteins (NFL) in the identification of neuronal damage. Patterns of NFL changes were almost identical in plasma and CSF, and both exhibited similar age-related increases in concentrations for HAD, MND and ANI, while avoiding the need for a lumber puncture.[27,28] This will enhance early diagnosis to improve quality of life, increase longevity, and arrest further deterioration of brain function.

Considering its treatability, the continuously high number of yearly transmissions and of migrants from

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endemic regions, the prevalence of HIV infection is bound to increase.4 The rising age of the HIV-infected population will make it ever more necessary to include non-HIV-associated forms of dementia into the differential diagnoses of HAND. As not all HIV patients will eventually suffer from HAND, specific parameters allowing for risk stratification would be helpful. This includes better instruments for screening and diagnosis. Because, for the time being, HIV cannot be eradicated from the body, improved ART substances as well as other principles of preventing and treating HAND are needed.

Strength & Limitations:

This study is one of the first attempt to establish association between CD4 cell count and HAND among diagnosed HIV positive adult patients in the eastern Indian state of Manipur which has 3rd highest HIV prevalence. The sample size scientifically calculated and also was adequate enough to establish the association. Though, the self-reported portion of the dataset might lead to recall bias that can under-represent the covariates. Also, the study was done in a small group with no randomization, so it may be difficult to apply the results on the general population.

CONCLUSION

Clinical disease of nervous system accounts for a significant degree of morbidity in a high percentage of patients with HIV infection. And this neurological problem is attributed to the pathogenesis process of HIV infection or secondary to opportunistic infections or neoplasms.

The study conducted among146 participants, it observed that 69 People living with HIV (47.26 %) had HIV associated neurocognitive disorder. Among the participants, the greater section 43.15% belonged to the Stage 1 category. Neurological involvement during HIV infection remains an important aspect of the infection requiring continued study and monitor. Cognitive decline can occur at the later stage of life and this might be accelerated by HIV infection further. It is important for the brain to function properly, so that a person can live with independence, leading a quality life. These ongoing efforts are directed to optimize this aspect of care for HIV patients. It is certain that multiple mechanisms contribute, and thus multiple therapeutic interventions will need to be rationally employed to achieve success in neuro cognitive manifestation of HIV infection.

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