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ORIGINAL RESEARCH

Study of spectrum of neurological manifestations among people living with hiv/aids and its association with CD4 count

[1]Dr. Baljinder Kumar, [2]Dr. Sumit Kumar, [3]Dr. Sulena, [4]Dr. Ravinder Garg, [5]Dr. Shubham, [6]Dr. Parampreet Singh, [7]Dr.Naveen

[1,5,7]Junior Resident, [2]Associate Professor, [3]Associate Professor, Division of Neurology, [4]Professor, [6]Senior Resident, Department of Medicine, GGS Medical College and Hospital, Faridkot, Punjab, India

Corresponding author
Dr.Sumit Kumar
Associate Professor, Department of Medicine, GGS Medical College and Hospital, Faridkot, Punjab, India

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Abstract

Aims and objectives: To study the spectrum of various neurological manifestations among PLHA. To evaluate the association of these neurological manifestations with CD4 count among PLHA.

Material and methods: This study will be conducted on PLHA presenting in ART centre, OPD and IPD in the Department of Medicine. It will be a hospital based cross-sectional study. The study will be carried out after approval from Institutional Ethics Committee, Guru Gobind Singh Medical College and Hospital, Faridkot. Written informed consent will be obtained from all the participants. A detailed clinical history and CNS examination for higher mental functions, MMSE, cranial nerve examination, reflexes, motor system and sensory system examination will be carried out. Patients will undergo routine haematological and biochemical investigations including CD4 count, along with other relevant test if required such as cerebro-spinal fluid (CSF) analysis,Computed tomography(CT) Head and Magnetic resonance imaging(MRI) brain, Nerve conduction velocity (NCV).HIV testing is done through ELISA.

Results: Mean age(years) of study subjects was 30.2 ± 5.9. Mean value of CD4 count(cells/mm³) of study population was 228.45 ± 167.63. Mean value of CD4 count(cells/mm³) of study population was 228.45 ± 167.63. Headache followed by fever was the most common presentations.TBM was the most common cns manifestation in 33% cases. Mean ± SD of CD4 count(cells/mm³) in patients without cryptococcus was 279.74 ± 169 which was significantly higher as compared to patients with cryptococcus (108.77 ± 82.47).(p value <.0001). Mean ± SD of CD4 count(cells/mm³) in patients with cranial nerve involvement was 300.88 ± 206.22 which was significantly higher as compared to patients without cranial nerve involvement (205.58 ± 147.78).(p value=0.014). Mean ± SD of CD4 count(cells/mm³) in patients with CVA was 311.78 ± 233.12 which was significantly higher as compared to patients without CVA (197.63 ± 124.28).(p value=0.021).

Introduction

Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is a global pandemic. As per the UNAIDS report on the global AIDS epidemic 2020 globally, an estimated 38.0 (31.6–44.5) million people were living with HIV in 2019(1).

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At the national level, estimated adult HIV prevalence (15-49 years) has declined since the epidemic's peak in 2000 where prevalence was estimated at 0.55% in 2000, through to 0.32% in 2010, and 0.21% in 2021. The northeast region States have the highest adult HIV prevalence (2.70% in Mizoram, 1.36% in Nagaland, and 1.05% in Manipur), followed by southern States (0.67% in Andhra Pradesh, 0.47% in Telangana, and 0.46% in Karnataka). The number of People Living with HIV (PLHIV) is estimated at around 24 lakhs. Southern States have the largest number of PLHIV viz. Maharashtra, Andhra Pradesh, and Karnataka are the top three(2).

HIV is transmitted primarily by sexual contact (both heterosexual and male to male), by blood and blood products, by infected mother to infants intrapartum, perinatally, or via breast milk; through injection drug use while sharing needles, syringes, occupational exposure to health care workers and laboratory workers. The hallmark of HIV disease is profound immunodeficiency resulting primarily from a progressive quantitative and qualitative deficiency of the subset of T lymphocytes referred to as helper T cells. The helper T cell is defined phenotypically by the presence on its surface of the CD4 molecule, which serves as a primary cellular receptor for HIV. Several mechanisms responsible for cellular depletion and/ or immune dysfunction of CD4+T cells have been demonstrated in vitro; these include infection and destruction of these cells by HIV, as well as indirect effects of immune clearance of infected cells, cell death associated with aberrant immune activation, and immune exhaustion due to aberrant cellular activation with resultant cellular dysfunction. CD4+T lymphocytes play a central regulatory role in the immune response. The decrease in CD4+T cells can compromise the normal immune functions of the body. Hence, the number of CD4+T cells in circulation provides important information regarding the immune competence of an individual (3).

Immune deficits associated with HIV result in infectious complications. The central mechanism is the progressive depletion of CD4 T lymphocytes, cells that are pivotal to the overall functioning of the immune system. In response to antigen presentation, they proliferate and release cytokines. Two of the most important are interleukin (IL)-2 and interferon (IFN) gamma. IL-2 stimulates cytotoxic T cells that eliminate viral infections, while IFN gamma stimulates antibody production in B cells and the cytotoxic effects of natural killer cells and macrophages to act against intracellular organisms. Impaired macrophage function consequent upon reduced IFN gamma production means that individuals with HIV infection are at particular risk both for primary and reactivated tuberculosis(9 4).

CD4 lymphocyte count is a marker for the likelihood of opportunistic infection. For individuals with a CD4 count consistently above 200 cells/ml the risk is low, but it increases as the CD4 count falls lower. Many of the organisms can cause infections but they are kept in abeyance while the immune system is competent, but re-emerge as immunosuppression progresses. Examples include herpes zoster, cytomegalovirus (CMV), and EBV. Others can be acquired de novo if the immune system is sufficiently compromised such as Pneumocystis jiroveci pneumonia, candidiasis, recurrent bacterial infection, wasting syndrome, cytomegalovirus, lymphocytic interstitial pneumonitis, tuberculosis, nontuberculousmycobacteriosis, and herpes simplex virus. (10-11).

As HIV and AIDS affect the immune system, the central nervous system (CNS) will suffer as well. Both HIV and AIDS induce various neurological problems, especially when HIV progresses and becomes AIDS. (12-13)

Conditions included in non-OPIs were seizures, ischemic stroke, aseptic meningitis, intracranial hemorrhage, vacuolar myelopathy, AIDS-associated dementia, GB syndrome, AMSAN, CIDP, mononeuritis multiplex cranialis, and dilated cardiomyopathy and Conditions included in OPIs were TB meningitis, cryptococcal meningitis, Pott's spine,

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multifocal leukoencephalopathy (PMLE), herpes zoster, herpes simplex, and cerebral toxoplasmosis(14).

CD4 T lymphocytes are a part of the human T-lymphocyte cells that are produced in the bone marrow and eventually mature in the thymus. They circulate in the body to fight against bacteria, viruses, and other organisms. If HIV goes untreated, the virus enters the cell and replicates, which eventually causes CD4 cells to die. The remaining infected cells release virions, which infect other cells, leading to the progression of the disease. The loss of CD4 T lymphocytes will result in the inability to have a proper immune response(15-16)

For a physician, the CD4 cell count has become the best indicator of disease progression and is used to stage disease and decline of CD4 T cells can lead to opportunistic infections, and it increases mortality(17).

As mentioned, the CD4 count is used to evaluate the progression of HIV. CD4 counts should be done on all patients first diagnosed with HIV disease. All HIV-positive patients are tested every 3 to 6 months. Results can offer insight into the possible diagnosis of AIDS and the risk of opportunistic infections. Additionally, the test is an indicator of treatment failure. Antiretroviral therapy (ART) should commence before CD4 levels are below 200 cells/mm^3, as complications are higher in this population of patients. Levels should be followed up every 3 to 6 months after starting ART to check for response to therapy. If the response is appropriate, the CD4 count can be rechecked every 6 to 12 months. Successful treatment is associated with an increase in CD4 count and adherence to therapy. With the use of ART, levels may increase by 100 to 150 cells/mm3 at the one-year mark(18-19).

Combination antiretroviral therapy (ART) has significantly reduced the morbidity and mortality resulting from HIV infection. ART is, however, unable to eradicate HIV, which persists latently in several cell types and tissues. Phylogenetic analyses suggested that the proliferation of cells infected before ART initiation is mainly responsible for residual viremia, although controversy still exists(21).

Aims and objectives

To study the spectrum of various neurological manifestations among PLHA.

To evaluate the association of these neurological manifestations with CD4 count among PLHA.

Materials and methods

This study was conducted on PLHA presenting in ART centre, OPD and IPD in the Department of Medicine. It is a hospital based cross-sectional study. The study was carried out after approval from Institutional Ethics Committee, Guru Gobind Singh Medical College and Hospital, Faridkot.

Written informed consent was obtained from all the participants. A detailed clinical history and CNS examination for higher mental functions, MMSE, cranial nerve examination, reflexes, motor system and sensory system examination will be carried out. Patients will undergo routine haematological and biochemical investigations including CD4 count, along with other relevant test if required such as cerebro-spinal fluid (CSF) analysis,Computed tomography(CT) Head and Magnetic resonance imaging(MRI) brain, Nerve conduction velocity (NCV).

Place of Study:Guru Gobind Singh Medical College and Hospital, Faridkot.

Type of Study: Hospital based cross sectional study

Type of Sampling: Non probability(convenience)sampling.

Study duration: June 2021 to June 2022

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Inclusion Criteria

- PLHA of any gender, and ≥18 years of age

Exclusion Criteria

- Any other confounding cause for neurological involvement such as epilepsy , parkinsonism
- Diabetes mellitus
- Patients not willing to give consent for the study.

Sample size

100 Patients

Results and observations

The study was conducted on PLHA presenting in, OPD and IPD in the Department of Medicine. 100 patients of PLHA of any gender, and ≥18 years of age were included in the study. Spectrum of various neurological manifestations among PLHA and CD4 count was studied and results are as follows.

Table 1:-Distribution of age(years) of study subjects.

Age(years)	Frequency	Percentage
18-20	3	3.00%
21-30	55	55.00%
31-40	37	37.00%
>40	5	5.00%
Mean ± SD	30.2 ± 5.9	
Median(25th-75thpercentile)	30(26-33.25)	
Range	18-54	

55(55.00%) patients belonged to age group 21-30 years followed by 31-40 years 37(37.00%) and >40 years 5(5.00%). Age group was 18-20 years of only 3 out of 100 patients (3.00%). Mean value of age(years) of study subjects was 30.2 ± 5.9 with median(25th-75th percentile) of 30(26-33.25). It is shown in table 1, figure 1.

Table 2:-Distribution of gender of study subjects.

Gender	Frequency	Percentage
Female	13	13.00%
Male	87	87.00%
Total	100	100.00%

87(87.00%) patients were males and 13(13.00%) patients were females.It is shown in table 2, figure 2.

Table 3:-Distribution of CD4 count(cells/mm^3) of study subjects.

CD4 count(cells/mm^3)	Frequency	Percentage
Stage 1 {>=500 cells/mm^3}	6	6.00%
Stage 2 {200-499 cells/mm^3}	44	44.00%
Stage 3{<200 cells/mm^3}	50	50.00%
Mean ± SD	228.45 ± 167.63	
Median(25th-75th percentile)	197.5(91.5-330.25)	
Range	19-967	

In majority 50(50.00%) of patients, CD4 count(cells/mm^3) was <200 cells/mm^3 followed by 200-499 cells/mm^3 44(44.00%). CD4 count(cells/mm^3) was >=500 cells/mm^3 of only 6 out of

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100 patients (6.00%). Mean value of CD4 count(cells/mm³) of study subjects was 228.45 ± 167.63 with median(25th-75th percentile) of 197.5(91.5-330.25). It is shown in table 3, figure 3.

Table 4:-Distribution of sign and symptoms of study subjects.

Sign and symptoms	Frequency	Percentage
Fever	77	77.00%
Headache	79	79.00%
Meningeal sign	55	55.00%
Altered sensorium	51	51.00%
Weakness	19	19.00%
Papilloedema	51	51.00%

Figure 4:-Distribution of sign and symptoms of study subjects.

In majority 79(79.00%) of patients, headache was present followed by fever 77(77.00%) , meningeal sign 55(55.00%) , altered sensorium 51(51.00%) and papilloedema 51(51.00%). Weakness was present in only 19 out of 100 patients (19.00%). It is shown in table 4,

Table 5:-Distribution of CNS manifestations of study subjects.

	CNS manifestations	Frequency	Percentage
Opportunistic infections	TBM	33	33.00%
	Bacterial meningitis	17	17.00%
	Cryptococcus	30	30.00%
	NCC	2	2.00%
	Toxoplamosis	3	3.00%
CNS manifestations	Cranial nerve involvement	24	24.00%
	CVA	27	27.00%
	Seizures	32	32.00%
	Hemi-paresis	12	12.00%
	HIV-associated neurocognitive disorder	1	1.00%

In majority 33(33.00%) of patients, CNS manifestation was TBM followed by seizures 32(32.00%), Cryptococcus 30(30.00%), CVA 27(27.00%), cranial nerve involvement 24(24.00%), bacterial meningitis 17(17.00%), hemi-paresis 12(12.00%), toxoplamosis 3(3.00%), NCC 2(2.00%) and HIV-associated neurocognitive disorder 1(1.00%) .
It is shown in table 5.

Table 6:-Distribution of peripheral manifestations of study subjects.

Peripheral manifestations	Frequency	Percentage
Peripheral neuropathy	22	22.00%
Myopathy	12	12.00%

In 22(22.00%) patients, peripheral manifestation was peripheral neuropathy and myopathy present only 12 out of 100 patients (12.00%). It is shown in table 6.

Table 7:-Association of CD4 count(cells/mm³) with fever.

CD4 count(cells/mm³)	Yes(n=77)	No(n=23)	Total	P value
Stage 1 {>=500 cells/mm³}	4 (5.19%)	2 (8.70%)	6 (6%)	0.317*
Stage 2 {200-499 cells/mm³}	37 (48.05%)	7 (30.43%)	44 (44%)	
Stage 3{<200 cells/mm³}	36 (46.75%)	14 (60.87%)	50 (50%)	

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Mean ± SD	234.7 ± 165.71	207.52 ± 176.05	228.45 ± 167.63	0.498†
Median(25th-75th percentile)	210(105-330)	134(84-327)	197.5(91.5-330.25)	
Range	19-967	32-631	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with fever. (Stage 1 {>=500 cells/mm³}:- 8.70% vs 5.19% respectively, Stage 2 {200-499 cells/mm³}:- 30.43% vs 48.05% respectively, Stage 3{<200 cells/mm³}:- 60.87% vs 46.75% respectively) (p value=0.317).

Mean ± SD of CD4 count(cells/mm³) in patients without fever was 207.52 ± 176.05 and in patients with fever was 234.7 ± 165.71 with no significant association between them. (p value=0.498). It is shown in table 7.

Table 8:-Association of CD4 count(cells/mm³) with headache.

CD4 count(cells/mm³)	Yes(n=79)	No(n=21)	Total	P value
Stage 1 {>=500 cells/mm³}	2 (2.53%)	4 (19.05%)	6 (6%)	0.007*
Stage 2 {200-499 cells/mm³	33 (41.77%)	11 (52.38%)	44 (44%)	
Stage 3{<200 cells/mm³}	44 (55.70%)	6 (28.57%)	50 (50%)	
Mean ± SD	202.76 ± 134.88	325.1 ± 236.05	228.45 ± 167.63	0.032†
Median(25th-75th percentile)	172(89.5-320)	334(144-431)	197.5(91.5-330.25)	
Range	32-600	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly higher in patients without headache as compared to patients with headache. (Stage 1 {>=500 cells/mm³}:- 19.05% vs 2.53% respectively, Stage 2 {200-499 cells/mm³}:- 52.38% vs 41.77% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly lower in patients without headache as compared to patients with headache. (Stage 3{<200 cells/mm³}:- 28.57% vs 55.70% respectively). (p value=0.007)

Mean ± SD of CD4 count(cells/mm³) in patients without headache was 325.1 ± 236.05 which was significantly higher as compared to patients with headache (202.76 ± 134.88).(p value=0.032) It is shown in table 8.

Table 9:-Association of CD4 count(cells/mm³) with meningeal sign(Kernig's sign, Brudzinski's sign, and nuchal rigidity).

CD4 count(cells/mm³)	Yes(n=55)	No(n=45)	Total	P value
Stage 1 {>=500 cells/mm³}	3 (5.45%)	3 (6.67%)	6 (6%)	0.285*
Stage 2 {200-499 cells/mm³}	28 (50.91%)	16 (35.56%)	44 (44%)	
Stage 3{<200 cells/mm³}	24 (43.64%)	26 (57.78%)	50 (50%)	
Mean ± SD	250.33 ± 170.02	201.71 ± 162.53	228.45 ± 167.63	0.15†
Median(25th-75th percentile)	231(119.5-330.5)	144(79-328)	197.5(91.5-330.25)	
Range	32-967	19-631	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with meningeal sign. (Stage 1 {>=500 cells/mm³}:- 6.67% vs 5.45% respectively, Stage 2 {200-499 cells/mm³}:- 35.56% vs 50.91% respectively, Stage 3{<200 cells/mm³}:- 57.78% vs 43.64% respectively) (p value=0.285).

Mean ± SD of CD4 count(cells/mm³) in patients without meningeal sign was 201.71 ± 162.53 and in patients with meningeal sign was 250.33 ± 170.02 with no significant association between them. (p value=0.15). It is shown in table 9.

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Table 10:-Association of CD4 count(cells/mm³) with altered sensorium.

CD4 count(cells/mm³)	Yes(n=51)	No(n=49)	Total	P value
Stage 1 {>=500 cells/mm³}	3 (5.88%)	3 (6.12%)	6 (6%)	0.15*
Stage 2 {200-499 cells/mm³}	27 (52.94%)	17 (34.69%)	44 (44%)	
Stage 3{<200 cells/mm³}	21 (41.18%)	29 (59.18%)	50 (50%)	
Mean ± SD	245.8 ± 149.89	210.39 ± 184.11	228.45 ± 167.63	0.293†
Median(25th-75th percentile)	267 (117-338.5)	143 (87-300)	197.5 (91.5-330.25)	
Range	32-600	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with altered sensorium. (Stage 1 {>=500 cells/mm³}:- 6.12% vs 5.88% respectively, Stage 2 {200-499 cells/mm³}:- 34.69% vs 52.94% respectively, Stage 3{<200 cells/mm³}:- 59.18% vs 41.18% respectively) (p value=0.15).

Mean ± SD of CD4 count(cells/mm³) in patients without altered sensorium was 210.39 ± 184.11 and in patients with altered sensorium was 245.8 ± 149.89 with no significant association between them. (p value=0.293)

It is shown in table 10.

Table 11:-Association of CD4 count(cells/mm³) with weakness.

CD4 count(cells/mm³)	Yes(n=19)	No(n=81)	Total	P value
Stage 1 {>=500 cells/mm³}	3 (15.79%)	3 (3.70%)	6 (6%)	0.027*
Stage 2 {200-499 cells/mm³}	11 (57.89%)	33 (40.74%)	44 (44%)	
Stage 3{<200 cells/mm³}	5 (26.32%)	45 (55.56%)	50 (50%)	
Mean ± SD	290.37 ± 196.08	213.93 ± 158.11	228.45 ± 167.63	0.073†
Median(25th-75th percentile)	328 (127-390)	172 (92-320)	197.5 (91.5-330.25)	
Range	19-631	32-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Figure 11:-Association of CD4 count(cells/mm³) with weakness. Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly higher in patients without weakness as compared to patients with weakness. (Stage 3{<200 cells/mm³}:- 55.56% vs 26.32% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly lower in patients without weakness as compared to patients with weakness. (Stage 1 {>=500 cells/mm³}:- 3.70% vs 15.79% respectively, Stage 2 {200-499 cells/mm³}:- 40.74% vs 57.89% respectively). (p value=0.027)

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But on analyzing quantitatively, mean ± SD of CD4 count(cells/mm³) in patients without weakness was 213.93 ± 158.11 and in patients with weakness was 290.37 ± 196.08 with no significant association between them. (p value=0.073). It is shown in table 11.

Table 12:-Association of CD4 count(cells/mm³) with papilloedema.

CD4 count(cells/mm³)	Yes(n=51)	No(n=49)	Total	P value
Stage 1 {>=500 cells/mm³}	3 (5.88%)	3 (6.12%)	6 (6%)	0.15*
Stage 2 {200-499 cells/mm³}	27 (52.94%)	17 (34.69%)	44 (44%)	
Stage 3{<200 cells/mm³}	21 (41.18%)	29 (59.18%)	50 (50%)	
Mean ± SD	245.75 ± 171.8	210.45 ± 162.97	228.45 ± 167.63	0.295†
Median(25th-75th percentile)	246 (112-330.5)	144 (89-321)	197.5 (91.5-330.25)	
Range	19-967	32-631	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with papilloedema. (Stage 1 {>=500 cells/mm³}:- 6.12% vs 5.88% respectively, Stage 2 {200-499 cells/mm³}:- 34.69% vs 52.94% respectively, Stage 3{<200 cells/mm³}:- 59.18% vs 41.18% respectively) (p value=0.15).

Mean ± SD of CD4 count(cells/mm³) in patients without papilloedema was 210.45 ± 162.97 and in patients with papilloedema was 245.75 ± 171.8 with no significant association between them. (p value=0.295). It is shown in table 12.

Table 13:-Association of CD4 count(cells/mm³) with TBM.

CD4 count(cells/mm³)	Yes(n=33)	No(n=67)	Total	P value
Stage 1 {>=500 cells/mm³}	1 (3.03%)	5 (7.46%)	6 (6%)	0.006*
Stage 2 {200-499 cells/mm³}	22 (66.67%)	22 (32.84%)	44 (44%)	
Stage 3{<200 cells/mm³}	10 (30.30%)	40 (59.70%)	50 (50%)	
Mean ± SD	252.52 ± 119.67	216.6 ± 186.47	228.45 ± 167.63	0.248†
Median(25th-75th percentile)	267 (187-330)	143 (80-331)	197.5 (91.5-330.25)	
Range	32-600	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 3{<200 cells/mm³} was significantly higher in patients without TBM as compared to patients with TBM. (Stage 1{>=500 cells/mm³}:- 7.46% vs 3.03% respectively, Stage 3{<200 cells/mm³}:- 59.70% vs 30.30% respectively).

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Proportion of patients with CD4 count(cells/mm³):- stage 2 {200-499 cells/mm³} was significantly lower in patients without TBM as compared to patients with TBM.. (Stage 2 {200-499 cells/mm³}:- 32.84% vs 66.67% respectively). (p value=0.006)
But on analyzing quantitatively, mean ± SD of CD4 count(cells/mm³) in patients without TBM was 216.6 ± 186.47 and in patients with TBM was 252.52 ± 119.67 with no significant association between them. (p value=0.248). It is shown in table 13.

Table 14:-Association of CD4 count(cells/mm³) with bacterial meningitis.

CD4 count(cells/mm³)	Yes(n=17)	No(n=83)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (7.23%)	6 (6%)	0.349*
Stage 2 {200-499 cells/mm³}	10 (58.82%)	34 (40.96%)	44 (44%)	
Stage 3{<200 cells/mm³}	7 (41.18%)	43 (51.81%)	50 (50%)	
Mean ± SD	244.53 ± 132.93	225.16 ± 174.39	228.45 ± 167.63	0.666†
Median(25th-75th percentile)	288 (143-340)	176 (89.5-329)	197.5 (91.5-330.25)	
Range	34-445	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with bacterial meningitis. (Stage 1 {>=500 cells/mm³}:- 7.23% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 40.96% vs 58.82% respectively, Stage 3{<200 cells/mm³}:- 51.81% vs 41.18% respectively) (p value=0.349).
Mean ± SD of CD4 count(cells/mm³) in patients without bacterial meningitis was 225.16 ± 174.39 and in patients with bacterial meningitis was 244.53 ± 132.93 with no significant association between them. (p value=0.666). It is shown in table 14.

Table 15:-Association of CD4 count(cells/mm³) with cryptococcus.

CD4 count(cells/mm³)	Yes(n=30)	No(n=70)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (8.57%)	6 (6%)	<.0001*
Stage 2 {200-499 cells/mm³}	2 (6.67%)	42 (60%)	44 (44%)	
Stage 3{<200 cells/mm³}	28 (93.33%)	22 (31.43%)	50 (50%)	
Mean ± SD	108.77 ± 82.47	279.74 ± 169	228.45 ± 167.63	<.0001†
Median(25th-75th percentile)	88.5 (66.25-121)	284 (160-348.5)	197.5 (91.5-330.25)	
Range	32-468	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly higher in patients without cryptococcus as compared to

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patients with cryptococcus. (Stage 1 {>=500 cells/mm³}:- 8.57% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 60% vs 6.67% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly lower in patients without cryptococcus as compared to patients with cryptococcus. (Stage 3{<200 cells/mm³}:- 31.43% vs 93.33% respectively). (p value <0.0001)

Mean ± SD of CD4 count(cells/mm³) in patients without cryptococcus was 279.74 ± 169 which was significantly higher as compared to patients with cryptococcus (108.77 ± 82.47).(p value <.0001). It is shown in table 15.

Table 16:-Association of CD4 count(cells/mm³) with NCC.

CD4 count(cells/mm³)	Yes(n=2)	No(n=98)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (6.12%)	6 (6%)	1*
Stage 2 {200-499 cells/mm³}	1 (50%)	43 (43.88%)	44 (44%)	
Stage 3{<200 cells/mm³}	1 (50%)	49 (50%)	50 (50%)	
Mean ± SD	246 ± 189.5	228.09 ± 168.23	228.45 ± 167.63	0.882†
Median(25th-75th percentile)	246 (179-313)	197.5 (90.5-329.5)	197.5 (91.5-330.25)	
Range	112-380	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with NCC. (Stage 1 {>=500 cells/mm³}:- 6.12% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 43.88% vs 50% respectively, Stage 3{<200 cells/mm³}:- 50% vs 50% respectively) (p value=1).

Mean ± SD of CD4 count(cells/mm³) in patients without NCC was 228.09 ± 168.23 and in patients with NCC was 246 ± 189.5 with no significant association between them. (p value=0.882). It is shown in table 20.

Table 17:-Association of CD4 count(cells/mm³) with toxoplamosis.

CD4 count(cells/mm³)	Yes(n=3)	No(n=97)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (6.19%)	6 (6%)	0.374*
Stage 2 {200-499 cells/mm³}	0 (0%)	44 (45.36%)	44 (44%)	
Stage 3{<200 cells/mm³}	3 (100%)	47 (48.45%)	50 (50%)	
Mean ± SD	129.67 ± 15.95	231.51 ± 169.29	228.45 ± 167.63	<.0001†
Median(25th-75th percentile)	134 (123-138.5)	207 (90-331)	197.5 (91.5-330.25)	
Range	112-143	19-967	19-967	

† **Independent t test,** * **Fisher's exact test**

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Distribution of CD4 count(cells/mm³) was comparable in patients without and with toxoplamosis. (Stage 1 {>=500 cells/mm³}:- 6.19% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 45.36% vs 0% respectively, Stage 3{<200 cells/mm³}:- 48.45% vs 100% respectively) (p value=0.374).

But on analyzing quantitatively, mean ± SD of CD4 count(cells/mm³) in patients without toxoplamosis was 231.51 ± 169.29 which was significantly higher as compared to patients with toxoplamosis (129.67 ± 15.95).(p value <.0001). It is shown in table 17

Table 18:-Association of CD4 count(cells/mm³) with seizures.

CD4 count(cells/mm³)	Yes(n=32)	No(n=68)	Total	P value
Stage 1 {>=500 cells/mm³}	3 (9.38%)	3 (4.41%)	6 (6%)	0.343*
Stage 2 {200-499 cells/mm³}	16 (50%)	28 (41.18%)	44 (44%)	
Stage 3{<200 cells/mm³}	13 (40.63%)	37 (54.41%)	50 (50%)	
Mean ± SD	246.94 ± 179.02	219.75 ± 162.64	228.45 ± 167.63	0.452†
Median(25th-75th percentile)	256.5 (73.5-380)	181.5 (101.5-328.5)	197.5 (91.5-330.25)	
Range	19-631	32-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Figure 18:-Association of CD4 count(cells/mm³) with seizures. Distribution of CD4 count(cells/mm³) was comparable in patients without and with seizures. (Stage 1 {>=500 cells/mm³}:- 4.41% vs 9.38% respectively, Stage 2 {200-499 cells/mm³}:- 41.18% vs 50% respectively, Stage 3{<200 cells/mm³}:- 54.41% vs 40.63% respectively) (p value=0.343).

Mean ± SD of CD4 count(cells/mm³) in patients without seizures was 219.75 ± 162.64 and in patients with seizures was 246.94 ± 179.02 with no significant association between them. (p value=0.452). It is shown in table 18.

Table 19:-Association of CD4 count(cells/mm³) with hemi-paresis.

CD4 count(cells/mm³)	Yes(n=12)	No(n=88)	Total	P value
Stage 1 {>=500 cells/mm³}	2 (16.67%)	4 (4.55%)	6 (6%)	0.157*
Stage 2 {200-499 cells/mm³}	6 (50%)	38 (43.18%)	44 (44%)	
Stage 3{<200 cells/mm³}	4 (33.33%)	46 (52.27%)	50 (50%)	
Mean ± SD	268.17 ± 198.22	223.03 ± 163.58	228.45 ± 167.63	0.384†
Median(25th-75th percentile)	267.5 (81.5-392.75)	189 (91.5-328.5)	197.5 (91.5-330.25)	
Range	19-600	32-967	19-967	

† **Independent t test,** * **Fisher's exact test**

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Distribution of CD4 count(cells/mm³) was comparable in patients without and with hemi-paresis. (Stage 1 {>=500 cells/mm³}:- 4.55% vs 16.67% respectively, Stage 2 {200-499 cells/mm³}:- 43.18% vs 50% respectively, Stage 3{<200 cells/mm³}:- 52.27% vs 33.33% respectively) (p value=0.157).

Mean ± SD of CD4 count(cells/mm³) in patients without hemi-paresis was 223.03 ± 163.58 and in patients with hemi-paresis was 268.17 ± 198.22 with no significant association between them. (p value=0.384). It is shown in table 19.

Table 20:-Association of CD4 count(cells/mm³) with cranial nerve involvement.

CD4 count(cells/mm³)	Yes(n=24)	No(n=76)	Total	P value
Stage 1 {>=500 cells/mm³}	2 (8.33%)	4 (5.26%)	6 (6%)	0.049*
Stage 2 {200-499 cells/mm³}	15 (62.50%)	29 (38.16%)	44 (44%)	
Stage 3{<200 cells/mm³}	7 (29.17%)	43 (56.58%)	50 (50%)	
Mean ± SD	300.88 ± 206.22	205.58 ± 147.78	228.45 ± 167.63	0.014†
Median(25th-75th percentile)	311 (156.25-380)	163.5 (87.75-320)	197.5 (91.5-330.25)	
Range	34-967	19-631	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly higher in patients without cranial nerve involvement as compared to patients with cranial nerve involvement. (Stage 3{<200 cells/mm³}:- 56.58% vs 29.17% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly lower in patients without cranial nerve involvement as compared to patients with cranial nerve involvement. (Stage 1 {>=500 cells/mm³}:- 5.26% vs 8.33% respectively, Stage 2 {200-499 cells/mm³}:- 38.16% vs 62.50% respectively). (p value=0.049)

Mean ± SD of CD4 count(cells/mm³) in patients with cranial nerve involvement was 300.88 ± 206.22 which was significantly higher as compared to patients without cranial nerve involvement (205.58 ± 147.78).(p value=0.014). It is shown in table 20.

Table 21:-Association of CD4 count(cells/mm³) with CVA.

CD4 count(cells/mm³)	Yes(n=27)	No(n=73)	Total	P value
Stage 1 {>=500 cells/mm³}	5 (18.52%)	1 (1.37%)	6 (6%)	0.002*
Stage 2 {200-499 cells/mm³}	14 (51.85%)	30 (41.10%)	44 (44%)	
Stage 3{<200 cells/mm³}	8 (29.63%)	42 (57.53%)	50 (50%)	
Mean ± SD	311.78 ± 233.12	197.63 ± 124.28	228.45 ± 167.63	0.021†
Median(25th-75th percentile)	330 (83-415.5)	171 (94-300)	197.5 (91.5-	

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			330.25)	
Range	19-967	32-560	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly higher in patients without CVA as compared to patients with CVA. (Stage 3{<200 cells/mm³}:- 57.53% vs 29.63% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly lower in patients without CVA as compared to patients with CVA. (Stage 1 {>=500 cells/mm³}:- 1.37% vs 18.52% respectively, Stage 2 {200-499 cells/mm³}:- 41.10% vs 51.85% respectively). (p value=0.002)

Mean ± SD of CD4 count(cells/mm³) in patients with CVA was 311.78 ± 233.12 which was significantly higher as compared to patients without CVA (197.63 ± 124.28).(p value=0.021)

It is shown in table 21.

Table 22:-Association of CD4 count(cells/mm³) with HIV-associated neurocognitive disorder.

CD4 count(cells/mm³)	Yes(n=1)	No(n=99)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (6.06%)	6 (6%)	1*
Stage 2 {200-499 cells/mm³}	0 (0%)	44 (44.44%)	44 (44%)	
Stage 3{<200 cells/mm³}	1 (100%)	49 (49.49%)	50 (50%)	
Mean ± SD	19 ± 0	230.57 ± 167.13	228.45 ± 167.63	0.211†
Median(25th-75th percentile)	19 (19-19)	200 (93-330.5)	197.5 (91.5-330.25)	
Range	19-19	32-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Distribution of CD4 count(cells/mm³) was comparable in patients without and with HIV-associated neurocognitive disorder involvement. (Stage 1 {>=500 cells/mm³}:- 6.06% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 44.44% vs 0% respectively, Stage 3{<200 cells/mm³}:- 49.49% vs 100% respectively) (p value=1).

Mean ± SD of CD4 count(cells/mm³) in patients without HIV-associated neurocognitive disorder involvement was 230.57 ± 167.13 and in patients with HIV-associated neurocognitive disorder involvement was 19 ± 0 with no significant association between them. (p value=0.211). It is shown in table 22.

Table 23:-Association of CD4 count(cells/mm³) with peripheral neuropathy.

CD4 count(cells/mm³)	Yes(n=22)	No(n=78)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (7.69%)	6 (6%)	<.0001*
Stage 2 {200-499 cells/mm³}	0 (0%)	44 (56.41%)	44 (44%)	
Stage 3{<200 cells/mm³}	22 (100%)	28 (35.90%)	50 (50%)	

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Mean ± SD	79.82 ± 47.33	270.37 ± 165.6	228.45 ± 167.63	<.0001†
Median(25th-75th percentile)	73 (38.5-99.5)	267.5 (134.5-343.5)	197.5 (91.5-330.25)	
Range	19-191	32-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly higher in patients without peripheral neuropathy as compared to patients with peripheral neuropathy. (Stage 1 {>=500 cells/mm³}:- 7.69% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 56.41% vs 0% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly lower in patients without peripheral neuropathy as compared to patients with peripheral neuropathy. (Stage 3{<200 cells/mm³}:- 35.90% vs 100% respectively). (p value <0.0001)

Mean ± SD of CD4 count(cells/mm³) in patients without peripheral neuropathy was 270.37 ± 165.6 which was significantly higher as compared to patients with peripheral neuropathy (79.82 ± 47.33).(p value <.0001). It is shown in table 23.

Table 24:-Association of CD4 count(cells/mm³) with myopathy.

CD4 count(cells/mm³)	Yes(n=12)	No(n=88)	Total	P value
Stage 1 {>=500 cells/mm³}	0 (0%)	6 (6.82%)	6 (6%)	0.0004*
Stage 2 {200-499 cells/mm³}	0 (0%)	44 (50%)	44 (44%)	
Stage 3{<200 cells/mm³}	12 (100%)	38 (43.18%)	50 (50%)	
Mean ± SD	51.17 ± 25.26	252.62 ± 164.22	228.45 ± 167.63	<.0001†
Median(25th-75th percentile)	43.5 (33.5-59.5)	231 (117.75-336.25)	197.5 (91.5-330.25)	
Range	19-94	32-967	19-967	

† **Independent t test,** * **Fisher's exact test**

Proportion of patients with CD4 count(cells/mm³):- stage 1 {>=500 cells/mm³}, stage 2 {200-499 cells/mm³} was significantly higher in patients without myopathy as compared to patients with myopathy. (Stage 1 {>=500 cells/mm³}:- 6.82% vs 0% respectively, Stage 2 {200-499 cells/mm³}:- 50% vs 0% respectively).

Proportion of patients with CD4 count(cells/mm³):- stage 3{<200 cells/mm³} was significantly lower in patients without myopathy as compared to patients with myopathy. (Stage 3{<200 cells/mm³}:- 43.18% vs 100% respectively). (p value=0.0004)

Mean ± SD of CD4 count(cells/mm³) in patients without myopathy was 252.62 ± 164.22 which was significantly higher as compared to patients with myopathy (51.17 ± 25.26).(p value <.0001). It is shown in table 24.

Discussion

The study was conducted in people living with HIV/AIDS (PLHA) presenting with central nervous system (CNS) manifestations, in Out patients and Indoor Department of Medicine.100 patients of PLHA of ≥18 years of age were included in the study. The spectrum

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of various neurological manifestations among PLHA and its association with CD4 count was studied.

In our present study, majority of (n=55,55.00%) patients belong to the age group 21-30 years followed by 31-40 years (n=37,37.00%) and 3 out of 100 patients (3.00%) belong to age group was 18-20 years. Mean age of study subjects was 30.2 ± 5.9.

A similar study showed that the maximum cases belonged to the age group of 31-40 years (28.0%), in contrast to our study where the maximum case belong to the age group 21-30 years(55%) (**15**) .Another study showed that (72.27%) of the age group 30 years to 49 years were affected, followed by 15y-29y of age group(**1**). Others studies have also shown similar results(16,17).

Males were common than female in our study male s to female ratio was 87:13.

Most studies had shown similar trends where males were predominantly present in comparison to female(1,9,**15**,**17**)

In our study majority 50(50.00%) of patients have CD4 count(cells/mm³) <200 cells/mm³ followed by 200-499 cells/mm³ 44(44.00%) . CD4 count(cells/mm³) was >=500 cells/mm³ of only 6 out of 100 patients (6.00%). Mean value of CD4 count(cells/mm³) of study subjects was 228.45 ± 167.63 with median(IQR) of 197.5(IQR =91.5-330.25).

Similar results were obtained compared to our study where the maximum number of cases 26 (52.0%) had a CD4 count of ≤ 150 cells/mm3. About 17 (34.0%) cases had a CD4 count of 151-300 cells/mm3. Only 7 (14.0%) had a CD4 count above 300 cells/mm3. In another study 55% of patients had CD4+ cells count below 200, 34% had CD4 cells count between 201 and 499, and 11% had CD4 cells count above 500 which is similar to our results (**15**,18).

CD4 count levels in patients with neurological symptoms ranged from 12 to 482 with an average of 115.1 in contrast to our mean value which was 228.45 ± 167.63. Similarly35% patients have CD4+T between 200-500/µl and 65% had <200/µl in contrast to our study which was 44% and 6% (**19**,20)

In the majority 79(79.00%) of patients, the headache was predominant complaint followed by fever 77(77.00%) , meningeal sign 55(55.00%) , altered sensorium 51(51.00%) and papilloedema 51(51.00%) . Weakness was present in only 19 out of 100 patients (19.00%). Similar trends were seen in the various studies done by other authors where headache was the predominant symptom(**19**,21).Though some studies showed that altered sensorium was predominant presentation in compare to our study(**15**,22).

In our study the most common opportunistic infections was TBM in 33(33%) cases followed bycryptococcal meningitis in 30(30%) and bacterial meningitis ,toxoplasmosis , NCC was observed in 17(17%), (3)3% and (2) 2% cases respectively .In the similar studies done by various authors showed the similar trend where TBM is the most common opportunistics infection which is followed by cryptococcal meningitis(15,23,24) . However study observed that Cryptococcalmeningitis(67.44%) was more common than TBM(18.60%)(25).

Most common cnsmanifestion was seizures 32(32.00%) followed by CVA 27(27.00%), cranial nerve involvement 24(24.00%), hemiparesis 12(12.00%), and HAND 1(1.00%) .

Various similar studies done by other authors have similar finding where seizure is found to be prominent cnsmanifestion(17,20,22). However other studies showed the dissimilar trend where CVAs were the commonest manifestation(9). Similarly cns stroke and cranial nerves involvement were predominant presentation(9,20).

Peripheral manifestation including myopathy and peripheral neuropathy were observed in our study i.e. 12% and 22% respectively. Similar finding of peripheral manifestation were observed by various authors(9,17,19).

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Conclusion

In our study majority of the patients of PLHA were the younger age group (21- 30 yr) with male predominance. The proportion of Opportunistic infection increases with a relative decrease in CD4 count. The most common infection was cryptococcal meningitis in PLHA with CD4 count below 200 cells/mm3. Headache followed by fever is the most common symptom and papilloedema in the most common sign in our study. It was also observed that peripheral manifestations were more common when the CD4 count dropped below 200/$mm^{3.}$

Limitationofstudy

Only 100 patients were included in the study, greater number of patient would have provided more information regarding the subject. Follow up of the patients was not done that might had provided the link between cd4 counts and mortality.

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