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ASSESSMENT OF THE NEUROLOGICAL MANIFESTATIONS IN PATIENTS DIAGNOSED WITH HIV AND TO ASSESS CD-4 COUNTS IN HIV PATIENTS

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ABSTRACT

Aim: The aim of the present study was to assess the neurological manifestations in patients diagnosed with HIV and to assess CD 4 counts in HIV Patients.

Methods: This study was conducted in the Department of Medicine and ART Center, Rajindra Hospital, Patiala. A total 200 patients in the time period 1st April to March 2021 were included in the study.

Results: Majority of patients were in economically productive age group 21-45 years. 70.50% patients were in 26-45 years of age group with mean age range 36.28±10.20. Out of 200 patients 55 (28.5%) had neurological manifestations. Among the 55 patients with neurological manifestations, majority (60.40%) were in 26-45 year age group with Mean age of study subjects: 36.28+ 10.20, Mean age for males: 34.30 ± 7.29, Mean age for females –29.27 ± 6.47and Male to female ratio : 2.56:1. Fever was the commonest symptom seen among the patients with neurological manifestations in 41 patients (71.93%) followed by altered sensorium seen in 36 patients (63.16%), head ache in 30 patients (52.63%), seizures in 15 patients (26.32%) of the patients. These results were statistically significant for all neurological symptoms except headache.

Conclusion:

Keywords: HIV infection, CD 4 counts, Neurological manifestations

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INTRODUCTION

Human immunodeficiency virus infection /acquired immuno-deficiency syndrome (HIV/AIDS) is a disease of the human immune system caused by infection with human immunodeficiency virus (HIV). The term "syndrome" has been used because AIDS does not constitute a single illness, but rather encompasses a wide range of clinical diseases including specific life-threatening infections and neoplasm's associated with a profound and irreversible acquired disorder of cell mediated immunity. Despite the impact of highly active antiretroviral therapy (HAART) on the morbidity and mortality associated with HIV infection, patients continue to ultimately have a dismal prognosis.[1]

The impact of the HIV/AIDS epidemic is already severe and continues to increase over the next decades. Globally there were 2.1 (1.9-2.4) million new HIV infections globally in 2017, showing a 33% decline in the number of new HIV infections since 2010. At the same time the number of AIDS deaths is also declining with 1.5 (1.4-1.7) million in 2013, down from 2.3 (2.1-2.6) million in 2005. National AIDS Control Organization estimated that 2.1 million people live with HIV /AIDS in India in 2017.During the past few decades AIDS has become a global health problem from 152 countries it is estimated that nearly 5 to 10 million people are infected worldwide with HIV 1. With a mean incubation period from time of infection to the development of AIDS of 8 to 10 years, It is projected that nearly all HIV 1 infected individuals will develop AIDS within the next 15 years.[2]

Any HIV infected individual with a CD4+ T cell count of less than 200/L has AIDS by definition, regardless of presence of symptoms of opportunistic disease. Neurological complications increase with decline in CD4+ T cell count. With CD4 T cell count less than 500/micro-L- Early stage -Demyelinating Neuropathy CD4 T cell count 200 to 500 – Mid stage-dementia VZV Radiculitis and CD4 T cell count less than 200 -Advance stage -Dementia, myelopathy, painful neuropathy. Plasma viral load independently provide an important prognostic information with regard to AIDS. If CD4 count goes below 250/microliter common neurological manifestations are TB meningitis (TBM), cryptococcal meningitis (CCM), progressive multifocal leukoencephalopathy (PMLE), AIDS dementia complexes (ADC), Acute inflammatory demyelination polyneuropathy (AIDP). HIV RNA (viral load) and CD4 T lymphocyte (CD4) cell count are the two surrogate markers of antiretroviral treatment (ART). Response and HIV disease progression that have been used for decades to manage and monitor HIV infection.[3-4]

Maharashtra is the most impacted state, according to sentinel surveillance, followed by Tamil Nadu.[5] The expected number of HIV/AIDS patients in India in 2019 is 2.14 million, and the adult HIV prevalence rate is 0.22%. Of the estimated overall number of HIV/AIDS patients, 39% of them are women and 3.5% are kids.[6] Significantly higher rates are observed among those who visit an STD clinic (3.6%), female sex workers (5.1%), those who use infected drugs (7.2%), and men who have sex with males (7.4%).(4) New HIV infections have decreased by 20% since 1999, when the global AIDS epidemic peaked, according to a UNAIDS study from 2010. 2.6 million individuals are thought to have contracted HIV in 2009, compared to 3.1 million in 1999.

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Adult HIV prevalence in India dropped from 0.36% in 2006 to 0.31% in 2009, a decline of more than 25% between 2001 and 2009. Compared to 2.5 million in 2001, 2.39 million individuals in India were living with HIV/AIDS in 2009. India had a 50% decrease in new cases since 2000, according to UNAIDS.

In India, the prevalence of HIV remains high among high-risk populations such as female sex workers, men who have intercourse with men, and injecting drug users, at 4.9%, 7.3%, and 9.2%, respectively.[7] According to a 2012 Punjab AIDS control society study, 0.18% of adults in Punjab are infected with HIV. The incidence of HIV is 0.25% in men and 0.18% in women. Up until October 2019, there were 52978 HIV positive cases enrolled for HIV care (pre-ART), and there were 36851 patients receiving ART overall.[8]

The aim of the present study was to assess the neurological manifestations in patients diagnosed with HIV and to assess CD 4 counts in HIV Patients.

MATERIALS AND METHODS

This study was conducted in the Department of Medicine and ART Center, Rajindra Hospital, Patiala. A total 200 patients in the time period 1st April to March 2021 were included in the study.

Inclusion criteria

1. Age more than 18 years
2. Previously or newly diagnosed HIV positive patients (ART and Pre-ART)

Exclusion criteria

1. HIV patients with past History of neurological diseases like cerebrovascular accidents, epilepsy, parkinsonism.
2. Comorbid conditions like diabetes mellitus.
3. Addiction of alcohol and other drug abuses like narcotics, sedatives, and hypnotics.

All patients and their relatives were informed about the study in their own vernacular language and written consent was taken. A detailed history was taken in every patient and recorded as per proforma given in the plan of the study.

STATISTICAL ANALYSIS

Data were entered and analyzed in SPSS data sheet version 23. Frequency tables and measures of central tendency (mean) and measures of dispersion (Standard Deviation) were calculated. Correlation was assessed using the chi-square test for comparing mean of different group independent sample t-test and ANOVA were applied. Karl Pearson correlation coefficient was calculated for measuring linear relationship between GGT level and other study variable.

RESULTS

Table 1: Association of HIV with Age Groups, Gender and Neurological manifestations

Age group	Frequency	Percentage
16-25	30	15%
26-35	74	37%

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36-45	67	33.50%
46-55	17	8.50%
56-65	12	6%
Gender		
Female	64	32%
Male	135	67.50%
Transgender	1	0.50%
Neurological manifestations		
Absent	145	71.50%
Present	55	28.50%
p value0.000		

Majority of patients were in economically productive age group 21-45 years. 70.50% patients were in 26-45 years of age group with mean age range 36.28±10.20. Among the 200 patients 64 were female and 135 were with Male to Female ratio of 2.11:1. Out of 200 patients 55 (28.5%) had neurological manifestations. Our results are statistically significant with p value 0.000.

Table 2: Age & Sex wise distribution of the study population (neurological manifestation)

Sr.No	Age Group	Male		Female		Total	
		Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
1.	21-25	4	7.02%	2	3.51%	6	10.53%
2.	26-35	18	31.58%	10	17.54%	28	49.12%
3.	36-45	17	29.82%	4	7.02%	21	36.84%
4.	>45	2	3.51%	0	0%	2	3.51%
Total		41	71.93%	16	28.07%	57	100%
Chi square = 15.89 p value = 0.860							

Among the 55 patients with neurological manifestations, majority (60.40%) were in 26-45 year age group with Mean age of study subjects: 36.28+ 10.20, Mean age for males: 34.30 ± 7.29, Mean age for females –29.27 ± 6.47and Male to female ratio: 2.56:1. These results were statistically not significant.

Table 3: Distribution of study subjects with Neurological symptoms

Sr. No.	Neurological Symptoms	Frequency	Percentage	χ^2	p value
1.	Altered Sensorium	39	68.42%	7.737	0.005
2.	Convulsions	15	26.32%	12.789	0.000

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3.	Vertigo	03	5.26%	45.789	0.000
4.	Cranial Nerve Abnormality	02	3.51%	49.281	0.000
5.	Sensory	03	5.26%	45.632	0.000
6.	Headache	30	52.63%	0.158	0.691
7.	Fever	41	71.93%	10.965	0.001
8.	Weight Loss	23	40.35%	2.123	0.145

Fever was the commonest symptom seen among the patients with neurological manifestations in 41 patients (71.93%) followed by altered sensorium seen in 36 patients (63.16%), head ache in 30 patients (52.63%) seizures in 15 patients (26.32%) of the patients. These results were statistically significant for all neurological symptoms except headache.

Table 4: Distribution of study subjects based on CNS findings

CNS Findings	**Frequency**	**Percentage**	χ^2	**p value**
Neck rigidity	23	43.86%	0.860	0.354
HMF	28	49.12%	0.018	0.895
Motor System	15	26.32%	12.789	0.000
Cranial	4	7.02%	42.123	0.000
Abnormal Fundus examination	12	21.05%	54.316	0.000
Gait	10	17.54%	0.158	0.691
Cerebellar	29	50.88%	3.947	0.047
Sensory	5	8.77%	19.263	0.000

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Plantar	27	47.37%	25.684	0.000

Neck rigidity was present in 23 (43.86%) patients out of 55 patients with neurological manifestations and 39 patients of meningitis, Higher mental function were abnormal based on MMSE score in 28 (49.12) patients, 15 (26.32%) patients had some abnormality in motor system examination, cranial nerve abnormality was observed in 4 (7.02%) patients (2 patient with UMN facial palsy, 2 patient had extra ocular muscle weakness in the form of iii, iv, vi cranial nerve involvement), 12 (21.05%) patients had abnormality on fundus examination, gait abnormality was observed in 10 (17.54%) patients, cerebellar signs could not be examined in 29 (50.88%) patients due to deranged HMF, 5 (8.77%) patients had abnormal sensory examination finding whereas planter reflex was abnormal in 27 (47.37%) patients (6 patients had unilateral extensor planter response, 6 patients had equivocal response and 15 patients had bilateral extensor planter response).

Table 5: Relation with CD4 count and neurologic illness (CD4 <200/mm3 & >200/mm3)

Diagnosis	**<200/mm^3**	**200-500/mm^3**	**Total**	**%**	**t-test (p value)**
TBM	15	10	25	47.37	8.02 (0.000)
CM	8	0	8	14.03%	6.40 (0.001)
BM	4	0	4	7.02%	1.72 (0.184)
AIDP	1	0	1	1.75%	00
PN	2	1	3	5.26%	3.52 (0.176)
PMLE	3	0	3	5.26%	4.22 (0.051)
Toxoplasmosis	2	0	2	3.51%	2.3 (0.239)
CVA	1	1	2	3.51%	00

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CTBLM	1	1	2	3.51%	00
HAD	5	0	5	8.80%	7.76 (0.004)
TOTAL	42	13	55	100%	

Most of the patients with neurological manifestations had CD4 count below 200/mm3. 10 cases of Tubercular meningitis, 1 case of peripheral neuropathy, 1 case of CVA and 1 case of cranial tuberculoma observed with CD4 count between 200-500/mm3. Results were statistically significant for TBM, CM, AIDP, CVA and HAD whereas insignificant for BM, PN, PMLE and Toxoplasmosis.

Table 6: Neurologic illness in relation to opportunistic and non- opportunistic cause

Neurologic illness	Types	Number (%) n=57
Non opportunistic or primary neurologic illness 11 (19.30%)	Peripheral neuropathy	3 (5.30%)
	HIV associated Dementia	5 (8.80%)
	AIDP	1 (1.80%)
	CVA	2 (3.50%)
Secondary to Opportunistic infection 44 (80.70%)	TBM	25 (47.37%)
	CM	8 (14%)
	BM	4 (7%)
	Toxoplasmosis	2 (3.50%)
	PMLE	3 (5.30%)
	CTBLM	2 (3.50%)

80.70% of all neurological manifestations were secondary to opportunistic infections whereas 19.30% cases were due to Primary illness related to HIV.

DISCUSSION

This study included 200 HIV positive patients registered in ART centre, Rajindra Hospital Patiala during the study period from 1st April 2021 to 31st March 2022.

In the present study, the age ranged from 21 to 51 yrs. Mean age was 36.28+ 10.20 year. Mean age of males was 34.30 ± 7.29 year and mean age of females was 29.27 ± 6.47year. Majority of the patients were in the economically productive age group of 20-45 yrs. The difference in the mean age was statistically not significant. Snider et al in their study of 50 cases found that the age range was 25 to 56 years in HIV reactive patients with neurological manifestations.[9] Dhadke et al in a study conducted at Solapur, India observed that maximum numbers of patients were in the age group 31-40 years and the median age at presentation was 37.5 years.[10]

33 patients out of 55 patients with neurological manifestations (61.4%) were either newly diagnosed or diagnosed after admission in medicine wards. The rest were already diagnosed at the time of admission and were on ART. Mc. Arthur et al reported that 10% of all AIDS patients

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in their study presented with complaints referable to the nervous system.[11] Levy et al in their study in San Francisco reported that 1/3 rd of their patients had neurological disorders as their presenting symptoms. Neurological disease was the 1st manifestation.[12]

Amongst the general symptoms fever was present in 39 (71.93%) out of 55 patients with neurological manifestations, and significant weight loss in approximately 40.35% (21 out of 55) patients which is comparable to a study done by Patel et al who observed that the commonest presenting symptom was fever (72.38%), followed by loss of weight (56.19%).[15] Altered sensorium was the commonest symptom seen in 34 patients out of 55 patients with neurological manifestations (63.16%), followed by head ache in 28 patients (52.63%), focal neurological deficit in 13 patients (26.32%) and seizures in 15 patients (26.32%) of the patients. The results of the present study were similar to Satyendra et al[13], Sharma et al[14] and Patel et al.[15]

CD4 Count was done in all the study subjects. 44 (77.19%) out of 55 patients with neurological manifestations had CD4 count <200/mm3 whereas 22.81% (13 out of 55) had CD4 count in 200-500/mm3. Mean CD4 count was 140.60 + 83.71. The lowest CD4 count was 28/mm3. Neurological manifestations those were seen in patients with CD4 count greater than 200/mm3 were tubercular meningitis in 10 patients, distal sensory axonal neuropathy in 1 patient and cranial tuberculoma in 1 patient. Our study is comparable to a study done by Dhadke et al which showed that 76% patient had CD4 count <200/mm3 whereas only 24% patient had CD4 count >200/mm3.[20] Hemant et al studied HIV patients with neurological complication had other opportunistic infections and most of these patients had CD4 count less than 200, Only 10 (20%) of patients had CD4 counts more than 200.[16] Satyendra et al in a study of 38 HIV-infected patients with neurological manifestations observed that the mean CD4 count was 177.9±105.0, of which 24 (63.2%) patients had CD4 count less than 200.[13] Sharma et al who did a study in 37 patients reported that in 13 (35.14%) patients CD4 Count was between 200-500/mm3 & <200/mm3 in 24 (64.86%) Patients.[14] The study conducted by Rana et al[17] and Patel et al[15] showed lower mean difference of neurological illness based on CD4 count as compared to the present study.

In the present study, 55 patients out of 200 patients (28.5%) were diagnosed to have neurological manifestations of HIV. This shows a high prevalence of neurological manifestation in HIV patients. Neurological complications were observed in 20.24 % of patients attending the outpatient clinic and in 44.57 % of in-patients in a study by Wadia et al in Pune.[18] In a study by Teja et al, an overall prevalence of 25.6% was obtained, which ranged from 15.8% in 1993 to 26.6% in 2003.[19]

The study has a few limitations that need to be mentioned. The total number of cases studied was only 200 HIV positive patients out of which 55 patients had neurological manifestations. Thus the study population included 55 HIV positive patients with neurological manifestations which is less as compared to the other major studies. Selection bias, which is a greater proportion of patients being in WHO stages 3 & 4 is another limitation, as the study was done in a tertiary care centre.

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CONCLUSION

The prevalence of HIV patients with neurological manifestation was 27.5 % over 12 month study period. Young adults were mainly affected. Opportunistic infections were the leading cause of neurological disorders in our study population. Central nervous system infections, intracranial mass lesions, stroke, and HIV-associated dementia were more common in patients with a CD4 count less than 200/mm3 but may occur in CD4 count between 200-500/mm3. High index of clinical suspicion of nervous system involvement in HIV patients at all stages help in early diagnosis and institution of specific therapeutic measures which in turn will decrease mortality and morbidity. This is a small study carried out over stipulated period of time in a small population and does not indicate the true incidence or prevalence of the disease in the community.

Due to cost constraints for opportunistic infections were done in limited number of patients and due to unavailability of PCR, stereotactic biopsy and other advanced investigating modalities all patients could not be investigated completely.

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