

**ORIGINAL RESEARCH****Neurological manifestations of HIV infection and it's correlation with CD 4 counts and viral load**

<sup>1</sup>Dr Sumit Thakur, <sup>2</sup>Dr.Arvind Gupta, <sup>3</sup>Dr. Jitendra Kanjolia, <sup>4</sup>Dr. Anugrah Dubay, <sup>5</sup>Dr. Sovran Rai, <sup>6</sup>Dr. Mayank Patidar,

<sup>1</sup>Consultant Physician, Care Multispeciality Hospital, Ashta, Sehore, M.P., India

<sup>2</sup>Associate Professor, Department of Neurology, Gajra Raja Medical College, Gwalior, M.P., India

<sup>3,4</sup>Senior Resident, Department of Neurology, Gajra Raja Medical College, Gwalior, M.P., India

<sup>5</sup>Medical Officer, District Hospital, Guna, M.P., India

<sup>6</sup>Consultant Physician, Arogyam clinic, Barwani, M.P., India

**Correspondence:**

Dr. Anugrah Dubay

Senior Resident, Department of Neurology, Gajra Raja Medical College, Gwalior, M.P., India

**Email:** [anuragh84@gmail.com](mailto:anuragh84@gmail.com)

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**ABSTRACT**

**Introduction:** 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.

**Aims & objectives:** - 1. To study the neurological manifestations in patients diagnosed with HIV.2. To study CD 4 counts in HIV Patients.3.To study viral load in patients of HIV.4.To study the correlation between neurological manifestations, CD 4 counts and viral load in HIV patients.

**Materials & methods:** This is a cross sectional study conducted over 86 patients of essential hypertension admitted in department of general medicine, R D Gardi medical college and C R Gardi Hospital, Ujjain (M.P) during the period from Jan 18 to June 19 after applying the inclusion and exclusion criteria.

**Observation and results:** In this study most common diagnosis was TBM 25 (56.8 %) patients having CD4 count  $\leq 100$  were having TBM,7(100%) patients having CD4 count  $\leq 100$  were having toxoplasmosis, 4 (66.7%) patients having CD4 count  $\leq 100$  were

having BM and 19 (43.2%) patients having CD4 count >100 were having TBM, 17 (100%) patients having CD4 count >100 were having peripheral neuropathy, 3 (75 %) patients having CD4 count ≤100 were having CVA.

**Discussion:** All patient with meningitis presented with headache vomiting and fever, focal neurological sign where absent none of these patients had convulsion, Diagnosis of meningitis done on basis of clinical symptoms, Fundoscopic examination was normal specific diagnosis was made on basis of CSF finding all patient had CSF examination had Indian ink preparation done. CSF finding reported in table. We had 44 cases of TBM the incidence of TBM has also found in other studies done by Mehta, *et al.* these is probably due to strong association of HIV and TB in India,

**Conclusion:** Neurological manifestations are seen with low CD4 count and high viral load in our study and there is a significant correlation between them hence can be stated that, these are the manifestations of the late stage of the disease, when the level of immunodeficiency has achieved a higher degree and which could result in high mortality.

**Keywords:** HIV infection, CD 4 counts, Neurological manifestations

## 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<sup>1</sup>.

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 (Quinn, 1990)<sup>1</sup>.

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<sup>3-4</sup>.

## AIMS & OBJECTIVES

1. To study the neurological manifestations in patients diagnosed with HIV
2. To study CD 4 counts in HIV Patients
3. To study Viral load in patients of HIV
4. To study the correlation between neurological manifestations, CD 4 counts and Viral load in HIV patients.

## MATERIALS & METHODS

This is a cross sectional study conducted over 86 patients of essential hypertension admitted in department of general medicine, R D Gardi medical college and C R Gardi Hospital, Ujjain (M.P) during the period from Jan 18 to June 19 after applying the inclusion and exclusion criteria

## INCLUSION CRITERIA

Patients above 20 years presenting with neurological manifestations and diagnosed to be HIV sero-positive by ICTC.

## EXCLUSION CRITERIA

Patients with pre-existing neurological disease before diagnosed as HIV Positive.

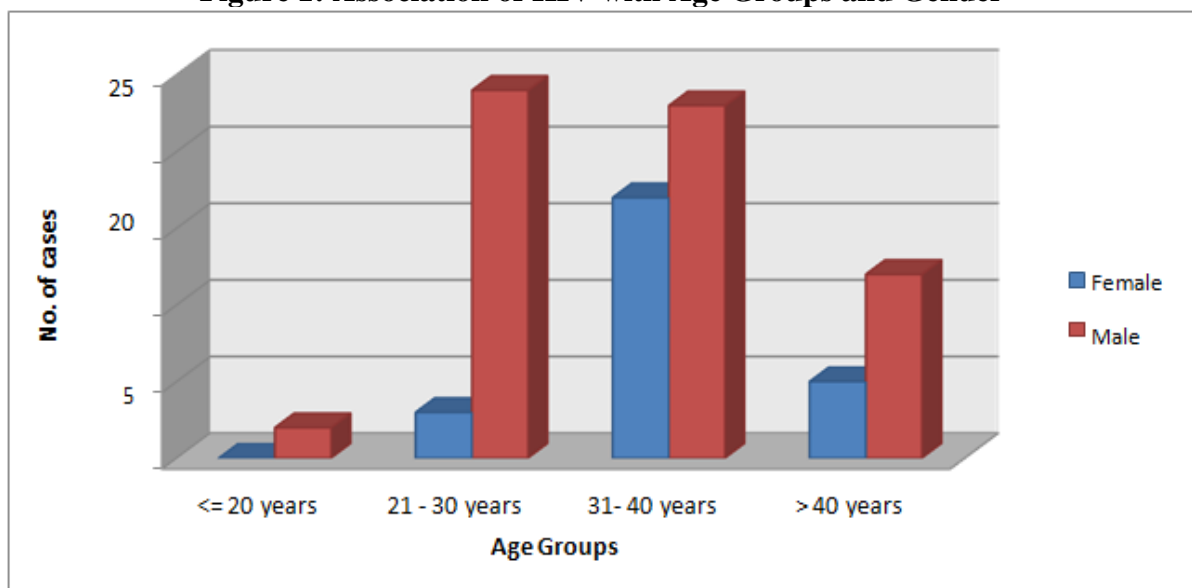
## STATISTICAL ANALYSIS

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.

## OBSERVATION AND RESULTS

In table-1, male patients are higher 61(70.9%) than female patients. Most common age group involve in this study is 31-40 years of age (40, 100%). Other age group involved  $\leq 20$  years there were no female and only 2 males, in the age group 21 - 30 years there were 3 females and 24 males(**Figure 1**)

**Figure 1: Association of HIV with Age Groups and Gender**



**Table 1: Association of HIV with Age Groups and Gender**

Age Groups	Gender		Total
	Female	Male	
<= 20 years	0(0.0%)	2(100.0%)	2(100.0%)
21 - 30 years	3(11.1%)	24(88.9%)	27(100.0%)
31- 40 years	17(42.5%)	23(57.5%)	40(100.0%)
> 40 years	5(29.4%)	12(70.6%)	17(100.0%)
Total	25(29.1%)	61(70.9%)	86(100.0%)
Chi-square=8.543, p=0.036			

Headache was the most common symptoms (75.5%) followed by fever (74.4%) and weight loss (72%). Focal neurological deficit in 5.8%, while convulsion was seen in 24.4%. Altered sensorium was seen in 45.3% (Table 2).

**Table 2: Distribution of study subjects based on symptoms**

Symptoms	Frequency (n)	Percentage %
Fever	64	74.4
Headache	65	75.5
Weight loss	62	72
Altered sensorium	39	45.3
Convulsion	21	24.4
FND	5	5.8

Sign of meningeal irritation were in 46 of cases. Higher motor functions were in 25 patients. Cranial nerve abnormality was seen only in 6 cases. While cerebeller in 4 patients (Table 3).

**Table 3: Distribution of study subjects based on CNS findings**

CNS findings	Frequency (n)	Percentage %
HMF	25	29
Cranial nerves	6	6.9
Meningismus	46	53.4
Cerebeller	4	4.6
Motor	19	22
Sensory	9	10.4

**Table 4: CD4 Level with Neurological Manifestation**

Diagnosis	CD4 Level				Total
	≤ 100		> 100		
BM	4	66.7%	2	33.3%	6
Crypto meningitis	2	100.0%	0	0.0%	2
CVA	3	75.0%	1	25.0%	4
Peripheral neuropathy	0	0.0%	17	100.0%	17
PML	0	0.0%	2	100.0%	2
TBM	25	56.8%	19	43.2%	44
Toxoplasmosis	7	100.0%	0	0.0%	7
Tuberculoma	3	75.0%	1	25.0%	4

In this study most common diagnosis was TBM 25 (56.8 %) patients having CD4 count ≤100 were having TBM,7(100%) patients having CD4 count ≤100 were having toxoplasmosis, 4 (66.7%) patients having CD4 count ≤100 were having BM and 19 (43.2%) patients having CD4 count >100 were having TBM,17(100%) patients having CD4 count >100 were having

peripheral neuropathy, 3 (75 %) patients having CD4 count  $\leq 100$  were having CVA (Table 4).

**Table 5: Viral load with Neurological manifestations**

Diagnosis	Viral load level				Total
	>20000		<20000		
TBM	4	66.7%	2	33.3%	6
Crypto meningitis	0	0.0%	2	100.0%	2
CVA	4	100.0%	0	0.0%	4
Peripheral	16	94.1%	1	5.9%	17
PML	2	100.0%	0	0.0%	2
TBM	24	54.5%	20	45.5%	44
Toxoplasmosis	2	28.57%	5	71.42%	7
Tuberculoma	0	0.0%	4	100.0%	4

In present study, TBM (20, 45.5%) was most common diagnosis followed by Toxoplasmosis (5, 71.42%) in patients having viral load  $< 20000$ . In patients having viral load  $> 20000$ , TBM (24, 54.5%) was most common diagnosis followed by Peripheral neuropathy (16, 94.1%) (Table 5).

## DISCUSSION

The present study consisted of 86 cases in which 51 (59.30%) were males and 25 (29.06%) were females. Other studies have status similar male preponderance Attili Venkata Satya et al. Predominance of Male cases may be due to migration to urban areas for job, staying away from families and promiscuous sexual habits resulting in acquiring HIV infection<sup>5</sup>.

Generally females particularly of low socioeconomic status who tend to avoid health checkups leading to a low detection rate. The age of patients of present study was varying from 19 years to 48 years. Most common number of patient was 31-40 years<sup>6</sup>.

In cases of meningitis headache was the commonest symptom in majority of patients, associated with vomiting and fever, Headache was diffused and intermittent. Headache seen in 45 patient that include 40 cases of tubercular meningitis, 1 case of cryptococcal meningitis and 4 cases of bacterial meningitis. fever was the next common symptom presented in 43 cases, fever was intermittent associated with headache and altered sensorium. In 21 cases all patient had generalized tonic clonic seizure, 4 patients were non epileptic who has on irregular treatment, 16 patient had meningitis and 5 patient had focal convulsion which turned out to be tuberculoma. 6 patients had cranial nerve palsy, 1 had Bell's palsy and remaining 5 had upper motor neuron lesion, 6<sup>th</sup> cranial nerve palsy associated with hemiparesis. Other investigation has also noted Bell's palsy associated with aseptic meningitis or due to lymphomatous meningitis also due to herpes zoster in our case no definite cause found for Bell's palsy<sup>7</sup>.

In present study the normal CD4 count is taken as 500-1200 cell/mm<sup>3</sup>. The mean CD4 count was 123.13 $\pm$ 93.035 in our study which was lower than the mean CD4 count in other studies was 150.28 in H.M Shah et al (2018), 172 $\pm$ 81.2 in Patel ML et al (2012), 432.58 $\pm$ 332.24 in Fitri FI et al (2016), 194.19 $\pm$ 96.45 PEDNEKAR S et al (2016). The reason behind this might be less compliance of patients to ART<sup>8</sup>.

In present study mean viral load was (24744.60 $\pm$ 15995.51) which was similar to study of Manesh A et al (2019) mean viral load is 2346.545 and median viral load was 20451.50 $\pm$ 15725.508 and was lower than a study conducted by Govender s. et al (2014) median viral load was 13000. In regression analysis it is found that viral load was significantly higher in patients with low CD4 count<sup>9</sup>.

All patient with meningitis presented with headache vomiting and fever, focal neurological sign where absent none of these patients had convulsion, Diagnosis of meningitis done on basis of clinical symptoms, Fundoscopic examination was normal specific diagnosis was made on basis of CSF finding all patient had CSF examination had Indian ink preparation done. CSF finding reported in table. We had 44 cases of TBM the incidence of TBM has also found in other studies done by Mehta, *et al.* these is probably due to strong association of HIV and TB in India, there are 2 cases of Cryptococcal meningitis presented with serious illness like convulsion and altered level of consciousness, in our study the prevalence of cryptococcal meningitis was low. All CSF where subjected to Indian ink preparation. On basis of CSF report. Satish Chandra *et al* study revealed cryptococcal meningitis in 37% cases, Deshpande *et al* and teja *et al* study found cryptococcal meningitis in 17% and 10.5% cases represent studies from various parts of the world show contrasting prevalence rates with marked geographical variations. In sub Saharan Africa, meningitis due to cryptococcus is more frequent then tuberculosis, Serology of all patient were positive<sup>10</sup>.

CNS toxoplasmosis was found in 7 cases in present study, In which 4 male 3 female. They presented with headache, fever and FND in neurology. In fundoscopic examination chorioretinitis presented in 7 patient, focal neurological deficient in 4 patients and 1 had hemiplegia. Serology in these patient is positive. Incidence of toxoplasmosis reported from various studies, Incidence to our studies in South American counties 40 to 60% seroprevalence of toxoplasma is notices. Peripheral neuropathy was found in 17 cases. Peripheral neuropathy was pure motor, sensory and mixed. Peripheral neuropathy was second most common neurological manifestation in this study. Causes are drug induced, diabetes, and HIV itself cause peripheral neuropathy. Peripheral neuropathy due to multiple factors, could not find the cause. Incidence in our studies similar to other studies. It was in accordance to Snider WD *et al* study found 16% cases. In contrary Levy *et al* found only in 6% cases. Peripheral neuropathy in HIV seropositive patients may be overlooked or misdiagnosed. A discerning clinical analysis may be helpful in the diagnosis of this common disease since the conventional electrophysiological study can underestimate some cases of peripheral nerve involvement<sup>11-13</sup>.

In this study 2 cases (2%) of progressive multifocal leukodystrophy were diagnosed. CSF examination normal, MRI suggestive of multifocal leukodystrophy. Our finding was similar to other studies. Levy *et al* reported 2% of their patients having PML and Snider WD reported in their 50 patients study 2 patients have PML. 4 cases of Tuberculoma was seen in my study, ring enhance lesion present suggestive of TBM in 4 cases. as dr. Murgesh Pastapur *et al* (2016) in 3 cases in his study and Attili *et al* study in Varanasi found CNS tuberculoma in 4% cases. 4 cases of Stroke with acute onset of hemiplegia, weakness associated with vasculitis and space occupying lesion, stroke related to HIV virus infection was found. Deshpande *et al* study shown stroke in 5% cases. Rajendra Singh *et al* study done in Punjab revealed stroke in 1.44% cases. 4 cases of Bacterial meningitis could not be differentiated on basis of clinical features, diagnosis made by CSF examination finding was seen in 4 patients in present study. Although bacterial meningitis is not one of the most common bacterial infections. Søggaard OS *et al* (2013) found HIV-infected patients the risk of bacterial meningitis in HIV-infected patients has been reported higher than the rest of the population<sup>14-16</sup>.

## CONCLUSION

Although the main and direct target of HIV infection are the cells of immune system, the nervous system is often damaged in course of infection, not only by the disease process that are secondary to immune dysfunction and its systemic manifestations but also by more fundamental effects of the retrovirus.

Neurological manifestations are seen with low CD4 count and high viral load in our study and there is a significant correlation between them hence can be stated that, these are the manifestations of the late stage of the disease, when the level of immunodeficiency has achieved a higher degree and which could result in high mortality. So monitoring and follow up is required in those cases to prevent subsequent morbidity and mortality. Co-morbidities were associated with poorer prognosis.

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