## **Research Article**

# NEUROLOGICAL MANIFESTATIONS OF HIV/AIDS: A CLINICAL PROSPECTIVE STUDY

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## ABSTRACT

Aims & Objectives: To study the clinical profile of neurological manifestations of Human immunodeficiency virus(HIV)/Acquired immunodeficiency syndrome(AIDS) and to correlate with the CD4+T lymphocyte count.Material & Methods : 50 patients who were in the age goup18-55 years, had HIV infection and history suggestive of Nervous system manifestations were included. The HIV patients with past/present history of other immunocompromised conditions ( cytotoxic drugs for malignancies, Post organ transplant patients, Patients using steroids for long term), previous history of epilepsy, focal neurological deficit and head injury were excluded from the study. All the patients were examined in detail by history and clinical neurological examination. For all the patients have done routine investigations, and specific investigations like CT/MRI Brain, Nerve Conduction Studies, CSF Analysis, EEG and Specific antibodies for organisms or parasite done only wherever it is required. All the patients were correlated with the CD4 T cell count.Results:: Among 50 patients, Commonest age group affected was 26-35 yrs with male predominance(62%). Most common symptom was non specific headache(38%). Most common opportunistic infetction was Tuberculous meningitis(34%). Toxoplasmsa encephalitis was the most common space occupying lesion(20%). More number of patients were seen in the CD4 range in between 51-200 cells/mic.L(72%) with all the diseases had correlation with CD4 T cell activityCONCLUSION: In the present study, Opportunistic infections were the leading cause in patients infected with HIV having Neurological manifestastions, usually occurs when the patients had severe immunosuppresion (CD4 count< 200 cells/µL).

Key words: HIV Positive patients, CD4 T cell count, Neurological manifestation

## **INTRODUCTION**

HIV infection is a global pandemic, with cases reported from virtually every country. In 2009, approximately 2.4 million people were estimated to be living with HIV/AIDS in India (AIDS epidemic update, 2010).Children (<15 years) account for 3.5% for all infection, while 83% are in the age group 15 to 49 years. The estimated adult HIV prevalence in India was 0.3% in 2009, with adult male prevalence 0.36% and female 0.25% in 2009 (0.25 to 0.39%) (NACO, 2010). It is estimated that India had approximately 0.12 million new HIV infection in 2009 (NACO, 2010).

Neurological manifestations are seen throughout the course of HIV disease from prodromal stage till terminal illness and all parts of neuroaxis can be involved. Symptomatic neurologic

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dysfunction develops in more than 50% of individual infected with HIV and neuropathological lesions are detected at autopsy in approximately 90% of cases. This may be explained by the fact that the central nervous system is a sanctuary site for HIV and there is poor penetration of antiviral drugs due to presence of intact brain barrier (Levy et al., 1985). The nervous system is among the most frequent and serious target of HIV infection occurring in patients with profound immune suppression. Cerebrospinal fluid (CSF) finding are abnormal in about 90% of patients even during asymptomatic phase of HIV infection (Fauci and Lane, 2008). Neurological problem is the first manifestation of symptomatic HIV infection in 10 - 20% of patients (HIV sentinel surveillance, 2007). Neurological manifestation may be either primary to pathological process of HIV infection or secondary to opportunistic infections or neoplasm. It may be inflammatory, demyelinating or degenerative in nature. The neurological manifestations, natural course and outcome of HIV disease is likely to be different in India from other countries because of prevailing endemic infections, poverty, illiteracy, inability to take anti-retroviral therapy (ART) and malnutrition.

The present study was carried out to assess the prevalence of various neurological manifestations in HIV positive patients, and its correlation with CD4 count.

## AIMS & OBJECTIVES:

- 1. To study the clinical profile of neurological manifestations of Human immunodeficiency virus(HIV)/Acquired immunodeficiency syndrome(AIDS)
- 2. To correlate with the CD4+T lymphocyte count.

## MATERIAL& METHODS:

This is a prospective study, which includes 50 cases of HIV positive patients who were presented to the outpatient department or admitted in KIMS Narketpally, with various neurological symptoms during the period of October 2008 to September 2010. After fulfilling the inclusion criteria all the patients were examined in detail by history followed by systemic examination specially for the central and peripheral nervous system. For all the patient done routine investigations like, complete blood picture, urine examination, random blood sugar, liver function tests, renal function tests, serum electrolytes, chest X ray PA view, ultrasonogram abdomen, VDRL, HIV status at ICTC by NACO guidelines and CD4 T cell count by flowcytometry. Some patients were underwent specific investigations like, CT/MRI Brain, Nerve Conduction Studies, CSF Analysis, EEG and Specific antibodies for organisms or parasite. Some of the patients were excluded from the study, as per the exlusion criteria which was given below. After conforming the specific diagnosis, all the diseases were correlated with CD4 T cell count to asses the severity.

## **INCLUSION CRITERIA:**

1. All adult (18-55 yrs) patients, admitted in medical wards and attending medical out patient department at KIMS, Narketpally, who were found to have HIV infection and history suggestive of Nervous system manifestations.

## **EXCLUSION CRITERIA:**

1. HIV patients with past/present history of other immuno compromised conditions like

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a)Patients on cytotoxic drugs for malignanciesb)Post organ transplant patientsc)Patients using steroids for long term

- 2. HIV patients with previous history of epilepsy
- HIV patients with previous history of epilepsy
   HIV patients with previous history of focal neurological deficit
- 4. HIV patients with previous history of head injury

## **OBSERVATIONS:**

#### Table 1: <u>Age distribution:</u>

| Age of the patient(Yrs) | No. of patients | Percentage |
|-------------------------|-----------------|------------|
| 18-25                   | 11              | 22.00      |
| 26-35                   | 21              | 42.00      |
| 36-45                   | 12              | 24.00      |
| 46-55                   | 06              | 12.00      |
| Total                   | 50              | 100        |

#### Table 2: <u>Sex distribution:</u>

| Age group         | Males | Percentage | Females | Percentage | Total |
|-------------------|-------|------------|---------|------------|-------|
|                   |       |            |         |            |       |
| 18-25Yrs          | 03    | 6.00       | 08      | 16.00      | 11    |
| 26.25Vng          | 17    | 34.00      | 04      | 8.00       | 21    |
| 20-35118          | 1/    | 34.00      | 04      | 0.00       | 21    |
| 36-45Yrs          | 08    | 16.00      | 04      | 8.00       | 12    |
| 16 55 yrs         | 03    | 6.00       | 03      | 6.00       | 06    |
| 40- <i>33</i> y18 | 03    | 0.00       | 03      | 0.00       | 00    |
| TOTAL             | 31    | 62.00      | 19      | 38.00      | 50    |
|                   |       |            |         |            |       |

## Table 3: Modes of transmission:

| Route                  | No. of patients | Percentage |
|------------------------|-----------------|------------|
| Sexual<br>transmission | 50              | 100        |
| Blood transmission     | 0               | 00         |
| Injection drug use     | 0               | 00         |

## Table 4: Presenting Neurological manifestations:

| Manifestations        | No of patients | Percentage |
|-----------------------|----------------|------------|
| Head ache             | 33             | 66.00      |
| Fever                 | 32             | 64.00      |
| Weakness of limb      | 17             | 34.00      |
| Neck stiffness        | 16             | 32.00      |
| Seizures              | 17             | 34.00      |
| Altered sensorium     | 13             | 26.00      |
| Sensory deficit       | 5              | 10.00      |
| Cognitive impairment  | 2              | 4.00       |
| Ataxia                | 1              | 2.00       |
| Sphincter disturbance | 1              | 2.00       |

## Table 5: <u>CD4+T cell count:</u>

| CD4+T cell count | No of patients | Percentage |
|------------------|----------------|------------|
| (cells/micro L)  |                |            |
| <50              | 2              | 4.00       |
| 51-200           | 36             | 72.00      |
| 201-500          | 12             | 24.00      |
| >501             | 0              | 00         |
| Total            | 50             | 100        |

## Table 6: Various Opportunistic infection:

| <b>Opportunistic infections</b>            | No of patients | Percentage |  |
|--|----------------|------------|--|
| Tuberculous meningitis                     | 17             | 34.00      |  |
| Toxoplasmosis                              | 10             | 20.00      |  |
| Tuberculoma                                | 5              | 10.00      |  |
| Cryptococal meningitis                     | 2              | 4.00       |  |
| Progressive multifocal leukoencephalopathy | 1              | 2.00       |  |
| Non-opportunistic infections               | 15             | 30.00      |  |
| Total                                      | 50             | 100        |  |

| CD4+T<br>cell count | Diagnosis                                       | No of Patients |
|---------------------|---|----------------|
| <50                 | Bilateral cerebellar infarcts                   | 1              |
|                     | Tuberculoma                                     | 1              |
| 51-200              | Tuberculous meningitis                          | 12             |
|                     | Toxoplasmosis                                   | 10             |
|                     | Aseptic meningitis                              | 5              |
|                     | Tuberculoma                                     | 4              |
|                     | Acute inflammatory demyelinating polyneuropathy | 3              |
|                     | Cryptococal meningitis                          | 2              |
|                     | Idiopathic epilepsy                             | 2              |
|                     | Progressive multifocal<br>leukoencephalopathy   | 1              |
| 201-500             | Tuberculous meningitis                          | 5              |
|                     | Recurrent transient ischemic attack             | 1              |
|                     | Potts spine                                     | 1              |
|                     | Cerebral infarct                                | 1              |
|                     | Acute inflammatory demyelinating polyneuropathy | 1              |
| >500                | No manifestations                               | 0              |

## Table 7: <u>Different neurological conditions at various levels of CD4+t cell count:</u>

## Table 8:<u>Mean CD4+Tcell countof patients with different neurological disease:</u>

| Disease  | Number of patients | Percentage | CD4+T Range<br>(Cells/mic.L ) | Mean CD4 T<br>Count |
|--|--------------------|------------|-------------------------------|---------------------|
|  |                    |            |                               | (Cells/mic. L)      |
| Tubeculous<br>Meningitis                             | 17                 | 34.00      | 71-276                        | 173                 |
| Toxoplasmosis  | 10                 | 20.00      | 102-264                       | 183                 |
| Tuberculoma  | 5                  | 10.00      | 48-148                        | 98                  |
| Cryptococcal<br>Meningitis                           | 2                  | 4.00       | 96-128                        | 112                 |
| Progressive<br>Multifocal<br>Leukoencephalop<br>athy | 1                  | 2.00       | 168                           | 168                 |
| Aseptic<br>meningitis                                | 5                  | 10.00      | 62-168                        | 115                 |
| Cerebrovascular<br>Accidents                         | 3                  | 6.00       | 41-215                        | 128                 |
| AIDP   | 4                  | 8.00       | 78-216                        | 147                 |
| Idiopathic<br>Epilepsy                               | 2                  | 4.00       | 163-208                       | 186                 |
| Potts spine  | 1                  | 2.00       | 265                           | 265                 |
| TOTAL  | 50                 | 100        |                               |                     |

## ANALYSIS:

The present study was carried out during the period of October 2008 to September 2010 at KIMS Narketpally. The study comprises of 50 HIV positive patients who were having the various neurological manifestations, of which more number of patients in the age group of 26-45 yrs (33patients) i.e.the age where people get contact with the infection and which the sexual life prevails (Table 1).

According to Table 2, Age group studied was 18-55 years out of which 31 patients were male(62.00%) and 19 are female patients(38.00%), out of them maximum of male patients are falling with in the age group of (26-45Yrs) and for females in the age group of (18-35Yrs).

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Table 3 indicates that 100% patients had contracted the disease sexually. Most of them have the history of multiple exposures i.e. heterosexual behaviour .No person contracted HIV through injection drug use. No patient had any history of receiving blood transfusion for the past 1 year.

As per Table 4, Out of 50 patients, most common presenting symptom is Headache 33 patients (66%), followed by Fever (64%), Weakness of limbs(34%) ,Seizures (30%), and least common is Ataxia (2%) and Sphincter disturbances (2%).

Table 5 shows that, Of the patients studied ,2 patients had CD4 count <50 cells/micro L (4%), 36 patients had CD4 count in between 51-200 cells/micro L (72%) ,12 patients had CD4 count in between 201-500 cells/micro L (24%) , no patients had CD4 count >500 cells/micro L.

According to Table 6, Out of 50 patients studied most common Opportunistic infection was Tuberculous meningitis (34%),followed by10 Toxoplasmosis (20%), Tuberculoma (10%) Cryptococcal meningitis (4%) ,and Progressive Multifocal Leukoencephalopathy (2%). 15 patients had Non-opportunistic infections(30%).

As per the Table 7, Tuberculous meningitis is the most common in CD4 count 51-200 (24%) followed by Toxoplasmosis(20%) and least is Progressive Multifocal Leucoencephalopathy(2%).CD4 count in the range between 201-500 again the tuberculosis was the predominant infection. There were no manifestations seen CD4 count more than 500.

The Table 8 depicts the mean CD4 count for the various manifestations. Patients with Tuberculous Meningitis had Mean CD4 count 173 cells/mm, Cryptococcal meningitis had Mean CD4 count 112, Toxoplasmosis Mean CD4 count 183,tuberculoma mean CD4 98 and patients with Progressive Multifocal Leukoencephalopathy had Mean CD4 count 168 cells/microL

Patients with Aseptic Meningitis had Mean CD4+T cell count 115 cells/mic.L, Cerebrovascular Accidents with 128 cell/mic.L, Acute Inflammatory Demyelinating Polyneuropathy 147 cells/mic.L, Idiopathic Epilepsy 186 cells/mic.L, and patient with Potts spine having 265 cells/mic.L.

## **DISCUSSION:**

HIV infection of the CNS results in damage to the nervous tissue and there has been a geometrical increase in the incidence and recognition of neurological disorders in HIV infected individuals over the past decade. As HIV-1 is a neurotropic virus, which can produce a large variety of neurological manifestations affecting all levels of the neuroaxis.

Neurological complications are detected in up to 60% of AIDS patients and are the result of direct HIV-1 infection, indirectly secondary due to opportunistic infections and neoplasms.

India has the second largest burden of HIV related pathology next to Sub- Saharan Africa. Neurological complications associated to HIV-1 infections, mainly due to clade C, are very common. The spectrum of HIV-1 associated complications reported within India appears to be different. Tuberculosis, Cryptococcosis and Toxoplasmosis are the major neuropathologies reflecting the endemicity and reactivation of latent infections, which is also seen in the present study.

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In the present study, the most common affected age group is 26-35 yrs, that is out of 50 patients 21 (42%), which is comparable to Sourab.et al(2006), 21 - 40 years(48%) and Kumar et al(2008), 25-49 years (40%).Among 50 patients, males are 31(62.0%) and 19 patients(38.0%) are Females with Male: Female is 1.63:1, which is also seen in Frogoso et al (1998), Male to Female ratio 1.94:1.

The most common route of transmission was heterosexual (100%). This finding correlated with Sourab et al(2006) and Deshpande et al (2005), (89.26% & 92.5% respectively) in which most common route of transmission was heterosexual. In the present study, found that the patients who had multiple sexual partners had a significant rate of positivity. Although Berenguer et al (1992), from USA noted that nearly 80 per cent of HIV-seropositive cases of TBM were IV drug users, in Indian series, HIV was acquired by heterosexual contact

Most of the patients presented with headache (66%) and fever (64%) as the most common complaint. This is also seen in studies conducted by the Satya et al (2006) (70% & 73% respectively) and Bolokadze et al (2008) (91% & 75% respectively). But the meningeal signs are more commonly seen in Satya et al(2006) when compared to the present study. Apart from the Idiopathic Epilepsy, seizures are most commonly due to focal brain lesions like Toxoplasmosis in Wong et al (1990),15.7% and in Dore et al (1996) 22%, followed by Meningitis(10% and 8% respectively), which is also seen in the present study (12% in Toxoplasmosis and 12% in Meningitis).

The most common opportunistic infection in the present study is Tuberculosis (44%) followed by the Toxoplasmosis (20%). When compared to Satya et al(2006), Tuberculosis (43.8%) is most common followed by the Cryptococcal meningitis (28.1%) which is done in patients around Varanasi (North India). According to Baradkar et al(2009), a review report of 2001, on the status of Cryptococcus in India strangely reveals more cases from Northern parts, where HIV prevalence is low compared to high HIV prevalent states in Southern or Western India. Since then overall scenario has not changed much. The discrepancy probably due to under reporting or misdiagnosis of cases. But in contrast Frogoso et al(1998), Toxoplasmosis is most commonly seen in the Western countries than Tuberculosis, as because of Tuberculosis is endemic in our country. In Deshpande et el(2005), Toxoplasmosis is more common than Tuberculosis, but the sample is very huge (300 cases) when compared to the present study.

Almost all of the diseases of Mean CD4 count, are well correlated with the studies conducted by the Satya et al(2006) and Deshpande et al(2005), except Tuberculoma and AIDP. In case of Tuberculoma, number of cases are more in the Deshpande et al (48 patients) when compared to the present study (5 patients). But in case of, AIDP the sample size remain same and in Deshpande et al Mean CD4 count (395 cell/ $\mu$ L) is high when compared to the present study (147cells/ $\mu$ L). According to DM Simpson.et al(1994), The condition generally occurs early in the course of HIV disease and may be the initial clinical disorder when seroconversion occurs. When AIDP occurs late in the course of HIV disease, in association with a low CD4 count, cytomegalovirus may be the primary etiologic agent. So in this scenario CMV may be the etiologic agent which is causing AIDP in the present study, which is unable to diagnose in our set up.

### **SUMMARY:**

- In the present study, Males (62.0%) are more commonly affected than Females (38.0%).
- Most commonly affected within the age group of 26-35 yrs (42.0%)
- The most common presenting of HIV with a neurological disease Non specific headache (66%).
- Most of the patients with seizures had a generalised tonic clonic seizures (88.2%).
- More number of patients(72.0%) are seen in the CD4 range in between 51-200 cell/mic.L
- Most common opportunistic infection is Tuberculous Meningitis (34.0%).
- Most common space occupying lesion in the CNS is Toxoplasmosis (20.0%).
- All the diseases had correlation with CD4+T lymphocye count.

## **CONCLUSION:**

Opportunistic infections of the nervous system are still by far the most commonly seen manifestation. Majority of the present study population were in advanced stage of HIV disease (AIDS), confirmed by clinical staging and CD4 level. Early detection and good prophylactic and therapeutic medications for these Opportunistic infections will reduce the mortality and morbidity in our country.

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