# Clinico-epidemiological profile of central nervous system manifestations in HIV patients

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## Abstract

**Introduction**: The neurologic complications of HIV infection are both common and diverse. The neurologic abnormalities in HIV infected individuals can be due either to opportunistic infections, neoplasm or to direct effects of HIV or its products. This research aims to study the frequency and clinical profile of neurologic disorders in HIV/AIDS and to study various infectious and non-infectious neurologic disorders in HIV/AIDS.

**Methodology:** We designed a cross-sectional study of all patients who were diagnosed with HIV were investigated to know about the neurological manifestations.

**Results:** During the study period we enrolled 108 HIV positive patients. Tubercular (TB) meningitis, cryptococcal meningitis, toxoplasmosis, tuberculoma, primary central nervous system (CNS) lymphoma and progressive multifocal leukoencephalopathy (PML) and peripheral neuropathy were the neurological manifestations seen.

**Conclusions:** Dysfunction of practically all segments of the nervous system is seen as a direct or indirect result of HIV itself or from opportunistic infections or neoplasm.

**Keywords:** HIV, AIDS, Nervous System, Opportunistic Infection.

## Introduction

The first description of acute human immunodeficiency virus (HIV) infection, a "mononucleosis-like" illness, was published in 1985. It has been estimated that 10 to 60% of individuals with early HIV infection will remain asymptomatic. However, the exact proportion is difficult to estimate since asymptomatic patients do not report to health professionals. A variety of symptoms and signs may be seen in association with acute symptomatic HIV infection. Published studies have consistently reported the most common findings like fever, lymphadenopathy, sore throat, myalgia/arthralgia, diarrhoea, weight loss, and headache.

The neurologic complications of HIV infection are both common and diverse. The virus disseminates to the central nervous system (CNS) during the initial days of systemic infection and can be detected in the cerebrospinal fluid (CSF) of most untreated patients thereafter. Nearly 40% of AIDS patients develop neurological complications during the course of their illness and about 10% experience neurological symptoms as the initial manifestations. The neurologic abnormalities in HIV infected individuals can be due either to opportunistic infections, neoplasm or to direct effects of HIV or its products. Patients who are asymptomatic and therefore not in contact with a medical professional may present with their first opportunistic infection in the CNS. Therefore, a thorough knowledge of the various presentation of CNS diseases in the HIV-infected patient is important. This research aims to study the frequency and clinical profile of neurologic disorders in HIV/AIDS and to study various infectious and non-infectious neurologic disorders in HIV/AIDS.

## Methodology

We designed a cross-sectional study of all patients who were diagnosed with HIV were investigated to know about the neurological manifestations. The study was conducted in the Department of Neurology. This is a 1500 bedded academic public hospital in Mumbai. Patients were diagnosed as HIV positive when they tested positive using enzyme-linked immunoassay on two separate occasions. Those samples with repeated positive results on the assay were sent for confirmation with Western Blot. These patients were approached and the purpose of the study was explained to them.

After obtaining their informed consent, we collected detailed socio-demographic information of these patients. We noted the clinical symptoms and signs of all patients. These patients underwent routine and specific investigations. Most of these investigations were performed on these patients as part of their routine clinical care. Patients underwent HIV viral load, CD4 count, cerebrospinal fluid examination, neuroimaging like computed tomography (CT) and magnetic resonance imaging (MRI), toxoplasma titre (Immunoglobulin G and M), cytomegalovirus titre (Immunoglobulin G and M), electromyography and nerve conduction studies. The investigations were ordered as deemed suitable by the treating physician and not necessarily for this research study. The diagnosis of various clinical manifestation was made by the treating physician based on the prevalent clinical criteria.The data was digitised in Epi Info statistical

software. Data verification and cleaning was done which was followed by description of data using frequencies and tables.

## Results

During the study period we enrolled 108 HIV positive patients. Of these 30 had neurological manifestations, 20 being males and 10 females. Half of these patients were in the age group 21-30 years.9 of these patients had meningitis, 10 of which had tubercular (TB) meningitis and 9 cryptococcal meningitis. Four patients were diagnosed with toxoplasmosis, two with tuberculoma and one with primary central nervous system (CNS) lymphoma and progressive multifocal leukoencephalopathy (PML) (Table 1). Three patients had peripheral neuropathy, of which two had distal type and one had acute inflammatory demyelinating polyneuropathy. Table 2 shows how different clinical features were observed in patients with different diagnosis. Fever and headache were the most common symptoms seen in our patients. Headache was seen in all patients of TB meningitis, cryptococcal meningitis, toxoplasmosis, tuberculoma and primary CNS lymphoma. Seizures were seen in 3 patients with toxoplasmosis, 3 patients of TB meningitis, 1 patient of cryptococcal meningitis and 1withtuberculoma.Signs of meningeal irritation were seen in all patients of TB meningitis and 4 patients of cryptococcal meningitis. We observed other clinical signs like impaired consciousness, focal defict, papilledema, distal sensory symptoms etc. Cerebrospinal fluid examination of patients with meningitis and neuropathy revealed high pressure (more than 200 mm water), high protein level (more than 45 mg/dL), low sugar (less than 40 mg/dL) in majority of the patients (Table 3). In patients with TB meningitis the CT and MRI showed basal exudates in 4 patients, hydrocephalus in 3 and cerebral edema in 2 patients (Table 4). In patients with cryptococcal meningitis the CT and MRI showed generalized cerebral edema in 5and hydrocephalus in one patient.In patients with toxoplasmosis, single ring enhancing lesion was seen in 3 patients on CT and in one patient in MRI and multiple ring enhancing lesions in 3 patients on MRI and in 1 patient on CT.

**Table 1: Various diagnosis of patients enrolled in our study**

| Neurological disorders in patients with HIV/AIDS | No. of patients |
|---|---|
| Total number of patients | **30** |
| **Meningitis** | **19 (63%)** |
| Tubercular Meningitis | 10 |
| Cryptococcal Meningitis | 9 |
| **Focal Cerebral Disease** | **8 (27%)** |
| Toxoplasmosis | 4 |
| Tuberculoma | 2 |
| Primary CNS Lymphoma | 1 |
| Progressive multifocal leukoencephalopathy | 1 |
| **Peripheral Neuropathy** | **3 (10%)** |
| Distal Symmetric Polyneuropathy | 2 |
| Acute inflammatory demyelinating polyneuropathy | 1 |

**Table 2: Clinical features of patients with different diagnosis**

| Clinical features | TBM* (n=10) | Crypto (n=9) | Toxo (n=4) | Tuber (n=2) | PCNSL (n=1) | PML (n=1) | DSP (n=2) | AIDP (n=1) |
|---|---|---|---|---|---|---|---|---|
| Fever | 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Headache | 10 | 9 | 4 | 2 | 1 | 0 | 0 | 0 |
| Vomit | 5 | 6 | 0 | 0 | 0 | 0 | 0 | 0 |
| Weight loss | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Seizures | 3 | 1 | 3 | 1 | 0 | 0 | 0 | 0 |
| Drowsiness | 4 | 4 | 1 | 1 | 0 | 0 | 0 | 0 |
| Visual Blurring | 2 | 4 | 1 | 1 | 0 | 0 | 0 | 0 |
| Meningeal irritation | 10 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| Impaired consciousness | 5 | 4 | 2 | 1 | 0 | 0 | 0 | 0 |
| Focal deficit hemiplegia | 1 | 0 | 2 | 1 | 1 | 1 | 0 | 0 |
| Papilledema | 3 | 7 | 1 | 1 | 0 | 0 | 0 | 0 |
| Distal sensory symptoms | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| Distal weakness | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Distal sensory loss | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| Areflexia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Extra CNS Tuberculosis | 5 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

*TBM: Tubercular meningitis; Crypto: Cryptococcal meningitis; Toxo: Toxoplasmosis; Tuber: Tuberculoma; PCNSL: Primary CNS Lymphoma; PML:Progressive multifocal leukoencephalopathy; DSP: Distal Symmetric Polyneuropathy; AIDP: Acute inflammatory demyelinating polyneuropathy

**Table 3: Cerebrospinal fluid examination findings in our study patients**

| Finding | TBM* (n=10) | Crypto (n=9) | DSP (n=2) | AIDP (n=1) |
|---|---|---|---|---|
| Pressure (>200 mm H20) | 6 | 7 | 0 | 0 |
| Proteins (>45 mg/dL) | 8 | 5 | 0 | 1 |
| Sugar (<40 mg/dL) | 8 | 4 | 0 | 0 |
| WBC (>200/ftL) | 7 | 2 | 0 | 0 |
| Acid fast bacilli | 2 | 0 | 0 | 0 |
| Cryptococcal antigen | 0 | 9 | 0 | 0 |
| India Ink Prep | 0 | 9 | 0 | 0 |

*TBM: Tubercular meningitis; Crypto: Cryptococcal meningitis; DSP: Distal Symmetric Polyneuropathy; AIDP: Acute inflammatory demyelinating polyneuropathy

**Table 4: Neuroimaging findings of patients with meningitis**

| Imaging modality | Tubercular Meningitis (n=10) | Cryptococcal Meningitis (n=9) |
|---|---|---|
| **Computed Tomography** | | |
| Hydrocephalus | 3 | 1 |
| Basal exudates | 4 | 0 |
| Edema | 2 | 5 |
| **Magnetic Resonance Imaging** | | |
| Hydrocephalus | 3 | 1 |
| Basal exudates | 4 | 0 |
| Edema | 2 | 5 |

## Discussion

Early reports described the clinical manifestations of neurological opportunistic infections and malignancies. With time, it appeared that distinct neurological syndromes like dementia and painful neuropathy also result from the HIV infection. Neurological manifestations become clinically apparent in only a few cases but neuropathological abnormalities are almost universally present in patients dying with AIDS, which suggests the subclinical pattern or underdiagnosis. Studies have shown that neurological complications can occur at any stage of HIV infection. Clinicians must also be aware that more than one site of neural axis can be involved at the same time.

Infection with Mycobacterium tuberculosis is a common complication of HIV infection among groups with a high prevalence of tuberculosis. As the HIV infection primarily impairs cell-mediated immunity, the immune response to TB bacilli in HIV infected individuals may be altered and the pathological-clinical features can be different than in HIV negative patients.We found the incidence of neurological manifestations of HIV to be 28%. The most common opportunistic infection of the CNS in our population was TB meningitis. Satishchandra et al in their study of 100 patients with neurological disorders associated with HIV infection had reported 24 (30%) cases of neurotuberculosis. The clinical features and CSF picture of patients in our study was similar to that reported by Berenguer et al.Their study however had higher prevalence of neurocognitive features. Cryptococcal meningitis is another commonly observed infection in our patients, although the incidence has decreased with the widespread use of anti-retroviral drugs.In the present study, cerebral edema was seen in 56% patients, hydrocephalus in 11% patients, and normal CT study in 33% patients. Satishchandra et al in their series of 37 patients of cryptococcal meningitis reported normal CT scan in 59.4% patients, cortical atrophy in 6.3%, hydrocephalus in 25% patients and cerebral edema in 9.4%.

We found four patients with Toxoplasmosis in our study. Toxoplasmic encephalitis was the most frequent CNS opportunistic infection in the pre-HAART era; it occurred in 10% patients or more, depending on the geographic origin. It is still very common in areas where HAART is not used widely.We found one patient of PML, whichis a late manifestation of AIDS and is seen in approximately 4% to 5% of patients with AIDS.Factors influencing a favorable outcome include higher CD4 counts, low viral load, undetectable JC virus in CSF following treatment, and contrast-enhancing lesions at time of diagnosis.

Apart from the infections, primary CNS lymphoma is considered an opportunistic neoplasm that is seen in approximately 5% of AIDS patients.The incidence of primary CNS lymphoma in HIV-infected individuals dropped substantially following highly active anti-retroviral treatmen in 1996, but now it appears to be rising again because of the increased life expectancy of HIV patients. Peripheral neuropathy is another common presentation in HIV infection and is clinically apparent in 15% to 25% patients.

## Conclusion

Dysfunction of practically all segments of the nervous system has been reported as a direct or indirect result of HIV itself or from opportunistic infections or neoplasm.The diagnostic process involves imaging, CSF examination and biopsy if needed. Our study has described the various clinical presentations HIV patients. Future studies should include patients from multiple centres to make the results more generalizable.

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