



THE CLINICAL SPECTRUM OF NEUROLOGICAL MANIFESTATIONS IN HIV/AIDS PATIENTS ATTENDING TERTIARY CARE CENTRE IN CENTRAL KERALA

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ABSTRACT

Background and Objectives : HIV is evolving as a major health hazard in India. Nervous system involvement in HIV patients is common and causes significant morbidity. We tried to elucidate the proportion and aetiologies of neurological involvement. **Methodology :** All patients above eighteen years and diagnosed to have HIV infection were included. Sample size calculated was 118. Patients having neurological involvement during study period were analysed. **Results :** Neurological involvement was observed in significant number (35.6%) of patients in younger age group (25-56 years) . 48.4% with newly detected HIV infection presented with neurological manifestations. Opportunistic infections (40.5%), of which Tuberculous Meningitis (64%), topped the underlying disorders. Stroke was present in 16.7% of cases. **Conclusion :** Nervous system involvement was observed to be more prevalent in young HIV patients and can be the initial manifestation. So young patients with neurological involvement like stroke should be screened for HIV.

KEYWORDS

HIV, Neurological involvement, Stroke

INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is a major health problem in many parts of the world including India. Neurologic disease was the first manifestation of symptomatic HIV infection in roughly 10-20% of persons, while about 60% of patients with advanced HIV disease had clinically evident neurologic dysfunction during the course of their illness. 2,3,4

In developing countries, opportunistic infections of the central nervous system account for most of the reported neurologic morbidity and mortality in AIDS. Studies from India have shown that neurotuberculosis is the most common opportunistic infection. We decided to conduct this study because there are only few studies depicting neurological manifestations in HIV/AIDS from this part of the country.

CASE STUDY**OBJECTIVES**

- 1.To determine the pattern of various neurologic manifestations of HIV/AIDS.
- 2.To compare the pattern of neurological involvement in our HIV/AIDS patients with those from other parts of India.

MATERIALS AND METHODS

All patients above 18 years of age, who were diagnosed to have HIV infection and presented to our hospital during the period of 18 months from January 2012 to June 2013, were included in the study. Sample size was calculated to be 118.

Inclusion criteria

Newly detected HIV cases and patients with known HIV seropositivity above 18 years of age, irrespective of whether on ART or not were included.

Exclusion criteria

HIV patients who were not willing to participate.
Patients with pre-existing neurological illness.

Methodolgy

All patients were interviewed for history of illness and a detailed examination was done, after getting written consent from the patient. Basic streamlined investigations were carried out for confirming the diagnosis, which included HIV ELISA, Western Blot and CD4 Count for all patients. CSF study, CT/MRI (Brain or Spinal Cord), serological markers etc were done according to the need. Data analysis was done

using SPSS version 16. The tests done were Chi-square test and Percentage analysis.

RESULTS

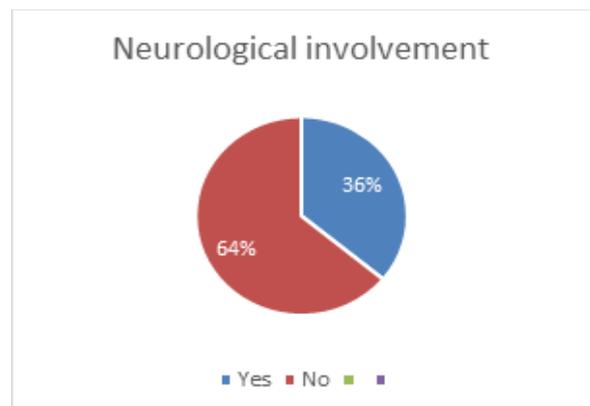
Age of the patients ranged from 28 to 60 years and mean age was 41.5 ± 6.16 years. The 68 males included in the study had mean age of 42.9 ± 5.96 years and 50 females in the study had mean of 39.6 ± 5.952 years (Table 1)

Table 1: Age and sex distribution

Sex	Number of cases	Age range	Mean age
Males	68	32-60	42.91
Females	50	28-54	39.6
Total	118	28-60	41.51

Out of 118, sixty eight patients (58%) were males and fifty cases were females (42%).

Out of 118 patients, 42 patients (35.6%) had neurological involvement.(Figure 1)

**Figure 1: Distribution of neurological involvement among cases**

Among the 42 patients with neurological manifestations, 27 were males and 15 were females. Male to female ratio was 1.8:1.

Common symptoms were fever, headache, altered mentation and focal

neurological deficits, of which headache was the most common. (Table 2)

Table 2: Distribution of symptoms among patients with neurological involvement

Symptoms	Opportunistic infections	CNS TB	Cryptococcosis	Toxoplasmosis	Primary CNS lymphoma	PML	Stroke	AND	Myelopathy	Peripheral nerve
Fever	12	8	4	3	0	0	2	0	0	0
Headache	17	11	4	5	2	1	4	0	0	0
Vomiting	8	7	4	0	1	0	2	0	0	0
Seizure	7	3	1	4	0	0	2	0	0	0
Altered mentation	8	6	3	1	1	1	2	7	0	0
Neck stiffness	11	7	3	1	0	0	1	0	0	0
Hemiparesis	3	3	0	0	0	0	6	0	0	0
Monoparesis	2	0	0	2	0	0	1	0	0	0
Paraparesis	0	0	0	0	0	0	0	0	3	1
Cranial nerve	4	3	0	1	1	0	6	0	0	0
Ataxia	3	2	0	1	1	1	2	1	0	0
Dementia	1	1	0	0	0	0	1	3	0	0
Depression	1	1	0	0	0	0	1	5	0	0

Papilloedema

Among 42 patients with neurological manifestations, 12 patients had papilloedema. Opportunistic infections were the commonest cause for papilloedema. 6 patients had CNS Tuberculosis, 2 had co-infection with TB Meningitis and Cryptococcosis, 2 had toxoplasmosis and 1 each had primary CNS lymphoma and Stroke. (Table 3)

Table 3: Causes for papilloedema

Causes	Percentage (%)
TB Meningitis	50
TBM + Crptococcal coinfection	17
Toxoplasmosis	17
Stroke	8
Primary CNS Lymphoma	6

Opportunistic infections were the most common CNS manifestations in our study, among which tuberculous meningitis was the commonest. A significant proportion of cases had peripheral nerve disease, HIV associated neurocognitive disease and cerebrovascular events. (Figure 2)

Out of 42 patients, seventeen (40.5%) had evidence of opportunistic infection (OI). Age of the patients ranged from 32 to 50 years with mean age of 39.9±4.53years. Out of 17 patients, 13 were males and 4 were females with male to female ratio of 3.25:1. Distribution of OI is shown in Table 4. Three patients had mixed infection.

Table 4: Distribution of opportunistic infections

Opportunistic Infections	Number of cases
CNS TB	11
Toxoplasmosis	5
Cryptococcosis	4

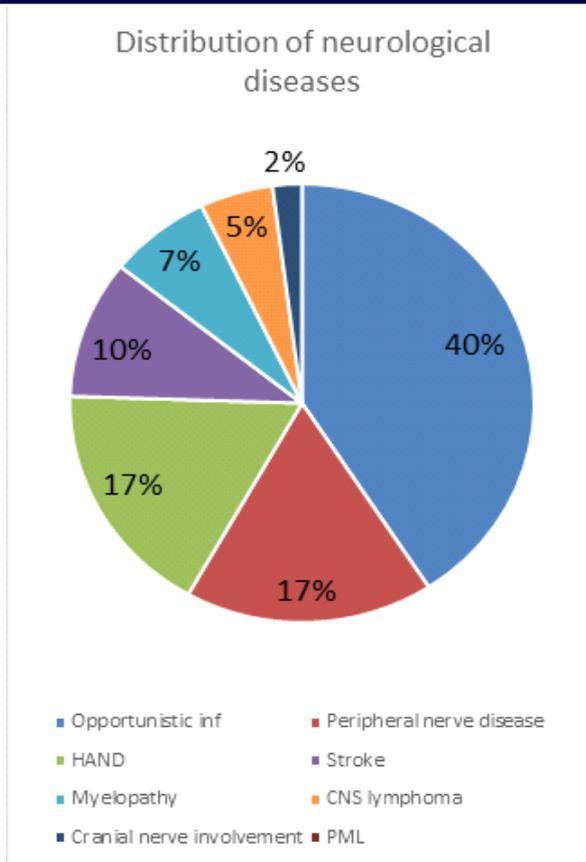


Figure 2 : Distribution of neurological diseases

Ten patients (23.8%) had Intra Cranial Space Occupying Lesions (ICSOL) in CT or MRI imaging. Five patients had single lesion and five patients had multiple ring enhancing lesions. Three cases were Tuberculomas, five were Toxoplasmosis and two primary CNS lymphomas. The two patients with primary CNS lymphoma were males with ages of 48 and 49 years.

One patient had Progressive Multifocal Leukoencephalopathy. The patient was a 35 year old unmarried female who presented with headache, unsteadiness of gait, altered sensorium and oral candidiasis.

Out of seven patients with stroke, three were males and four were females. Female to male ratio was 1.3:1. Age of the patients who had stroke, ranged from 35 to 43 years with mean age of 38 years.

Three male patients had spinal cord involvement and all of them presented with paraparesis. Age of the patients ranged from 40 to 48 years. MRI Spine showed evidence of possible vacuolar myelopathy.

Seven patients (16.7%) had peripheral nerve disease. Four patients had distal symmetric sensory neuropathy, two had mononeuritis multiplex and one patient had distal symmetric sensory motor polyneuropathy. None of the patients had demyelinating polyradiculopathy or CMV radiculitis.

Out of the 42 patients, eight patients (19.05%) had evidence of HIV Associated Neurocognitive Disorder (HAND). Age of the affected patients ranged from 34 to 56 years with mean age of 44.25±8.1 years. Of the eight, three were males and five were females. Seven patients were newly detected HIV cases. Three patients had HIV Associated Dementia (HAD) and five had Minimal Neuro Cognitive Disorder (MNCD).

ART status of the patient and neurological involvement

Out of 118 HIV patients included in the study, 63 were newly detected HIV seropositive cases, 10 patients were aware of their HIV seropositive status, but not on any treatment due to various reasons and 45 patients were on Anti Retroviral Treatment. (Figure 3)

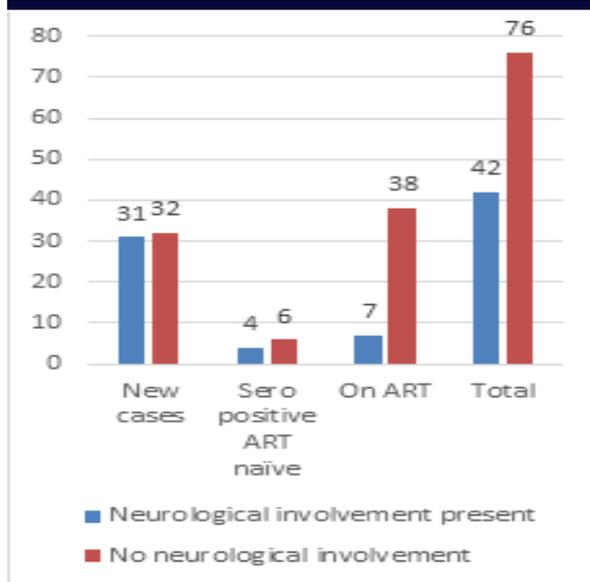


Figure 3: ART status of the patient and neurological involvement

DISCUSSION

Globally, 36.7 million [30.8–42.9 million] people were living with HIV at the end of 2016. 1 This study is aimed at studying the neurological manifestations in HIV patients attending our hospital.

In this study, 118 cases of HIV patients were included. Regarding age distribution, similar findings as that of our study were noted by Abhinav Gupta et al 5 and Mc Arthur et al.6 Age of HIV patients with neurological manifestations ranged from 25-56 years in the study by Snider WD et al, which was comparable with our study. 2 Male to female ratio was 1.36:1 in our study.

In our study, 42 patients (35.6%) had neurological manifestations. Satyendra K Sonkar et al reported 40% prevalence of neurological manifestations which was akin to ours.5

Out of 42 patients, 27 were males and 15 were females. This shows a greater prevalence of neurological manifestations in males, with male to female ratio of 1.8:1. Comparable to our result, Sherita Chapman et al reported male to female ratio of 1.2:1.7

Common symptoms in our study were headache, fever, altered mentation and focal neurological deficits. Headache was the most common symptom, observed in 28 cases (66.7%). Most of the patients with opportunistic infections, CNS lymphomas and stroke complained of headache. S K Sharma et al also noted headache as the commonest neurological symptom (62.5%).8 Fever was another common symptom (34%) noticed mainly in patients with opportunistic infections. Similar report of fever as a common symptom was documented in studies done by Pal et al and Satyendra K Sonkar et al. 5,9

Altered sensorium was also common. Most patients with altered mentation had either OIs or HAND. Satyendra K Sonkar et al and Wadia et al also reported altered sensorium as an important presentation.5,10 Focal neurological deficits were in the form of hemiparesis in seven, monoparesis and paraparesis in three each. Close to our results Satyendra K Sonkar et al5 and Sharma et al7 also reported focal neurological deficits in HIV cases. Ten patients had cranial nerve involvement. Facial nerve was affected in majority of cases.

Out of 118 cases, 64 cases were detected to have HIV infection for the first time on admission. Of the 64 new cases, 31 patients had neurological manifestations (48.4%). Ten patients were aware of their HIV positive status, but were not taking any regular treatment.

Of the 42 HIV patients with neurological manifestations, OIs including CNS Tuberculosis, Cryptococcal Meningitis and Toxoplasmosis were the most common diagnoses. 17 patients had

opportunistic infections (40.5%), 2 had Primary CNS Lymphoma caused by EBV, 1 had Progressive Multifocal Leukoencephalopathy. Seven had cerebrovascular events (6 thrombotic stroke and 1 hemorrhagic stroke), ten had cranial nerve involvement, eight had HAND, which included both AIDS Dementia Complex(ADC) and Minimal Neurocognitive Disorder (MNCD), three had myelopathy and seven had peripheral nerve involvement. Wadia et al reported similar manifestations in thier study.10 Very similar to our study, Teja et al reported that meningitis was the most common CNS infections (39.4%), followed by mass lesions (27.5%).11 Tuberculous Meningitis was the most common opportunistic infection observed. CNS Tuberculosis (64%) was followed by Cerebral Toxoplasmosis (29%) and Cryptococcal Meningitis (23%). Comparable results were reported by Satyendra Sonkar et al and Sharma et al. 5,7

Tuberculous meningitis was the most common opportunistic infection seen. 11 patients had evidence of CNS Tuberculosis. Tubercular meningitis was common (48.9%) in the study by Satyendra K Sonkar et al .5 Sircar et al observed that tuberculosis was present in 54.8% of their patients.12

Of the 17 patients with CNS opportunistic infections, 4 patients had evidence of cryptococcal meningitis and 5 had cerebral toxoplasmosis. There were no cases of Herpes Encephalitis or CMV Encephalitis in this study, similar to the studies by Satyendra et al and Wadia et al. 5,10

We had 2 cases of Primary CNS lymphoma caused by EBV. Snider et al reported that 3 out of 50 patients had Primary CNS lymphoma.2 Levy et al reported that 4.1% of patients had Primary CNS Lymphoma.4 One unmarried female patient with history of multiple sexual partners was diagnosed to have PML. Ten patients (23%) had space occupying lesions in CT/MRI imaging. Three cases were Tuberculomas, five were Toxoplasmosis and two had primary CNS lymphoma.

Stroke was present in 16.6% of patients (7/42 cases). Stroke was a common neurological manifestation in this study. Age of the patients with stroke ranged from 35 to 43 years with mean of 38. Out of 7 patients who had stroke, 3 were males and 4 were females. Female to Male ratio was 1.3:1. Andre Mochan et al in their study of 35 HIV patients with stroke observed that mean age was 32.1 years and female to male ratio of 1.5:1. 13 In five out of seven patients, stroke was the first presentation of HIV infection (71.4%).

Three patients had spinal cord involvement, all the 3 presented with paraparesis. This study report of 3 cases of myelopathy (7.1%) was higher compared to studies from other parts of India. 5,11 Seven patients had evidence of peripheral nerve disease.

Eight patients had HIV associated Neurocognitive disorder (HAND). Three patients had HIV associated dementia and five had MNCD. Depression was seen in five patients and dementia in three patients with HAND.

Close to this study result, Satyendra K Sonkar et al reported that 9.3% patients presented with HAND.5 Study by Navia et al from the west have shown that 20–30% of patients with advanced HIV infection go on to develop AIDS Dementia Complex which is comparable.14

Comparison of our study with international studies

CNS tuberculosis was the most common involvement in our study unlike studies from West (Table 5), the reason probably being the high prevalence of tuberculosis in general population of India. Non infectious complications like stroke, HAND and peripheral nerve disease were high in this study.

Table 5 : Comparison of our study with international studies

Neurological Disease	Our study (n=42)	Levy et al 2 (n=315)	Snider et al 4 (n=50)	Mc Arthur et al 6 (n=186)
CNS TB	26%	<1%	0	1%
Cryptococcosis	9.5%	13%	4%	6%
Toxoplasmosis	11%	32%	10%	8%
Primary CNS lymphoma	4.8%	10%	14%	17%

PML	2.4%	2%	4%	0
Stroke	16.6%	1.5%	6%	<1%
Cranial nerve involvement	4.8%	3%	0	2.1%
HAND	16.6%	0	0	7.3%
Myelopathy	7%	—	—	—
Peripheral nerve disease	16.6%	6%	16%	5%

Comparison of our study with other Indian studies

Pattern of various neurological disorders in HIV in this study was comparable with studies from other parts of India. (Table 6)

Table 6: Comparison of our study with other Indian studies

Neurological disease	Our study(n=42)	Satishchandra etal(n=100)15	Satyendra etal(n=43)5	S K Sharma etal(n=45)8
Meningitis	30%	61%	67%	45%
ICSOL	15%	—	7%	5%
PML	2%	1%	2%	0%
Stroke	16%	1.5%	7%	7.5%
HAND	16%	4%	10%	—
Myelopathy	7%	—	3%	-
Peripheral nerve disease	16%	65	5%	20%

CONCLUSIONS

A significant percentage of HIV patients (35.6%) in our study had nervous system involvement and were young. Males outnumbered females. Headache was the commonest symptom followed by fever, altered mentation and focal neurological deficits.

This study revealed that neurological manifestations can be the initial presentation in HIV infection. So young patients presenting with neurological diseases should be screened for HIV. Opportunistic infections especially Tuberculous meningitis was the most common. Stroke was an important manifestation of HIV infection in young adults. So HIV in young adults may be recognised as an independent risk factor for stroke.

REFERENCES:

- UNAIDS. Report on the Global AIDS Epidemic 2016.
- Levy RM, Bredesen DE, Rosenblum ML. Neurological manifestations of the acquired immunodeficiency syndrome (AIDS): experience at UCSF and review of the literature. *J Neurosurg*. 1985 Apr;62(4):475-95
- Koppel BS, Wormser GP et al. Central nervous system involvement in patients with acquired immune deficiency syndrome (AIDS). *Acta Neurol Scand*. 1985 May;71(5):337-53.
- Snider WD, Simpson DM, Nielsen S, Gold JW et al. Neurological complications of acquired immune deficiency syndrome: analysis of 50 patients. *Ann Neurol*. 1983 Oct;14(4):403-18.
- Satyendra K Sonkar, Abhinav Gupta, Virendra Atam et al. Clinical profile of neurological manifestation in Human Immunodeficiency Virus-positive patients. *N Am J Med Sci*. 2012 November; 4(11): 596-599.
- Mc Arthur JC. Neurologic manifestations of AIDS. *Medicine (Baltimore)* 1987;66:407-37.
- Sherita Chapman, Misan Pessu, Elizabeth Chimah et al. Neurological Manifestations in HIV-Positive African American Population *Journal Neurology*. 2012;125:258-9.
- Sharma SK, Dwivedi NC, Kumar N, Bharti A, Meena LP. Neurological manifestation of HIV infection in North-Eastern part of India.. *Natl J Physiol Pharm Pharmacol*, [cited November 25, 2013]; Online First: 13 Jun, 2013. doi: 10.5455/njppp.2014.4.130620131
- Pal J, Karmakar PS, Ray A, Saha S, Roy K, Talukdar A, et al. Opportunistic infections of central nervous system in AIDS. *J Indian Med Assoc*. 2009;107:446-9.
- Wadia RS, Pujari SN, Kothari S, Udhar M, Kulkarni S, Bhagat S, et al. Neurological manifestations of HIV Disease. *J Assoc Physicians India*. 2001;49:343-8.
- Teja VD, Talasila SR, Vemu L. Neurologic Manifestations of HIV infection: An Indian hospital based study. *Indian J Med Res*. 2005;121:377-94.
- Sircar AR, Tripathi AK, Choudhary SK, Misra R. Clinical profile of AIDS: A study at a referral hospital. *J Assoc Physicians India*. 1998;46:775-8.
- Andre Mochan et al. Stroke in Black South African HIV-Positive Patients. *Stroke*. 2003;34:10-15.
- Navia B, Jordan BD, Price RW. The AIDS Dementia Complex: Clinical features. *Ann Neurol*. 1986;19:517-24.
- Satishchandra P, Nalini A, Gourie-Devi, M et al. Profile of neurological disorders associated with HIV/AIDS from South India (1989-1996). *Indian J Med Res* 2000;111: 14-23.