



A STUDY ON NEUROLOGICAL MANIFESTATIONS IN HIV PATIENTS

General Medicine

Dr. S. Lakshmi Bai Prof & HOD, Department of General Medicine**Dr. M. Bharath krishna Kumar** Post Graduate, Department of General Medicine**Dr. Mohammad Arif Shaikh*** Md, Dept Of General Medicine *Corresponding Author

ABSTRACT

Background: Clinical disease of the nervous system accounts for a significant degree of morbidity in a high percentage of patients with HIV infection. The neurologic problems that occur in HIV-infected individuals may be either primary to the pathogenic processes of HIV infection or secondary to opportunistic infections or neoplasms. Among the more frequent opportunistic diseases that involve the CNS are toxoplasmosis, cryptococcosis, progressive multifocal leukoencephalopathy, and primary CNS lymphoma. Other less common problems include mycobacterial infections; syphilis; and infection with CMV, herpes zoster, HTLV-1, Trypanosoma cruzi, or Acanthamoeba. **Aim:** Identifying various neurological manifestations occurring in HIV patients, their co-relation with the CD4 count and incidence. **Materials And Methods:** This study done in 100 HIV patients admitted in general wards and MICU between March 2021 to September 2022 in the department of general medicine. **Results:** Of the 100 patients, 35 had neurological manifestations. Following were the neurological manifestations: Tuberculous meningitis (25.7%), cerebrovascular complications (2.9%), pyogenic meningitis (5.7%), seizure disorders (11.4%), AIDS dementia complex (22.9%), cryptococcal meningitis (14.3%), progressive multifocal leukoencephalopathy (2.9%), Tuberculoma (2.9%). The most common manifestation was neurotuberculosis. It was associated with high mortality rates in the patient. **Conclusions:** The incidence of neurological manifestations was around 35% in our study. Headache and altered sensorium were the two common symptoms observed in this study. Most of the patients in our study had a heterosexual transmission of disease. Neurological manifestations in men are more common than in women. Meningitis caused by tubercle bacilli was the most common disease in this study group, and the next was the cryptococcal meningitis. Many of the patients who had the disease were of young age. Many of the patients had expired. No significant CD4 count correlation was found between the patients with neurological manifestations and those without neurological manifestations. Patients with neurological manifestations had high mortality and poor outcome. Tuberculous and pyogenic meningitis were associated with very high mortality. CD4 count of low had increased mortality. Patients with coexisting tuberculous meningitis and HIV had significantly lower CD4 counts. Of the 100 patients, 35 had neurological manifestations.

KEYWORDS

Neurological manifestations, HIV and AIDS.

INTRODUCTION

The neurological manifestations of HIV consist of CNS complications caused directly by H.I.V., including cognitive disorders and other CNS diseases such as myelopathy and the demyelinating neuropathies, and secondary disorders caused by opportunistic infections, neoplasm cerebrovascular events, as also the effects of metabolic derangements and medications. Genetic factors will influence the risk of neurological side effects due to HIV drugs. Neurological complications are also due to damage caused by the virus itself and due to HIV and AIDS, such as cancers associated with these diseases. Some of the drugs used to treat H.I.V. and AIDS can also cause neurological complications while attempting to control the virus's rapid spread.

The prevalence was 20.24% of patients attending the out-patient clinic and in 44.57% of inpatients. The most common manifestation was herpes zoster meningitis and mass lesion which was studied in India. In the developed countries, that is at Georgia laboratory investigations. CNS Neurological complications were detected in 76 patients; 13 patients had two or more neurological complications. Tuberculosis meningitis was the most common neurological disorders 26 (34%), followed by CNS toxoplasmosis 17 (22%), cryptococcal meningitis 11 (15%), presumed CMV encephalitis 5 (7%), PML 4 (5%), primary CNS lymphoma 4 (5%) and bacterial meningitis 3 (4%).

AIM

Identifying various neurological manifestations occurring in HIV patients, their co-relation with the CD4 count and incidence.

OBJECTIVES

Primary Objective: - Identifying various manifestations occurring in HIV patients.

Secondary Objective: - To find the incidence of neurological manifestations in HIV patients.

Study Design: Prospective simple randomized cross sectional study.

Study Setting: This study was done at the Government General Hospital, Kadapa.

Study Subjects: Patients admitted to General Medicine Department,

Government General Hospital, Kadapa

Sample Size: 100

Study Period: March 2021 to September 2022

Inclusion Criteria

HIV patients admitted at Government General Hospital were considered for the study

Exclusion Criteria

All the less than 16 yrs. of age.

Patients who did not consent to be part of the study.

Immunocompromised state due to other reasons.

Criteria For Diagnosis:

Ethical Clearance: Before collection of data, all subjects were briefed about the purpose of the study and written informed consent was obtained. All investigations were done free of cost and no financial burden imposed on the patient. Ethical clearance was obtained from the institutional ethics committee.

Statistical Analysis: All the data was initially entered into Microsoft Excel, and later these spreadsheets were used for analysis. Statistical analysis was done by using S.P.S.S. version 20.0.

Descriptive statistics were calculated as frequency, percentage, mean and standard deviation. Descriptive data were represented using various tables, graphs, diagrams. For all the statistical tests of significance, a p-value of <0.05 was considered to reject the null hypothesis. For categorical nominal variables, the Chi-square test was done to test the association between the variable

RESULTS

Incidence

35 Patients had neurological manifestations among the 100 patients that were considered. The incidence of the neurological manifestations was 35%.

Table No. 1 clinical features and its distribution

Clinical Presentation	Patients	%
International Journal of Scientific Research		7

Headache	20	55.6
HEM	2	5.6
ALTERED	8	22.2
SEIZURES	4	11.1
PARAPARESIS	1	2.8
QUADRAPARES	0	0.0
PARESTHESIA	1	2.8

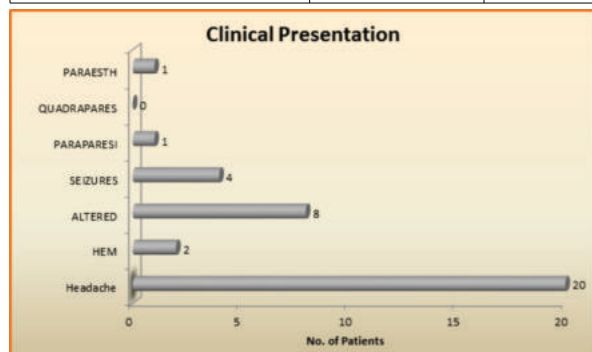


Chart No. 1 Clinical Features And Its Distribution

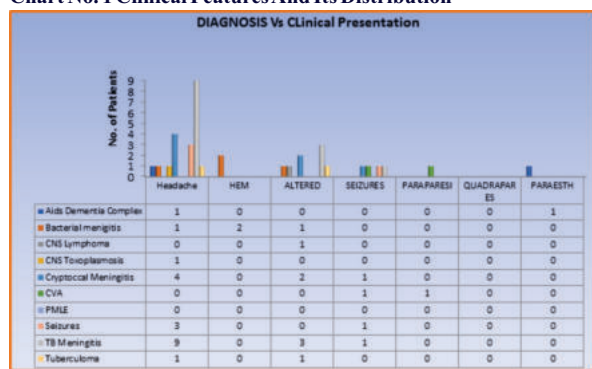


Chart No. 2 Diagnosis Vs Clinical Presentation

Table No 3 Various Neurological Manifestations And Its Incidence

DIAGNOSIS	No. of Patients	%
AIDS DEMENTIA COMPLEX	8	22.9
BACTERIAL MENINGITIS	2	5.7
CNS LYMPHOMA	1	2.9
CNS TOXOPLASMOSIS	3	8.6
CRYPTOCOCCAL MENINGITIS	5	14.3
CVA	1	2.9
PALE	1	2.9
SEIZURES	4	11.4
TB MENINGITIS	9	25.7
TUBERCULOMA	1	2.9
Total	35	100.0

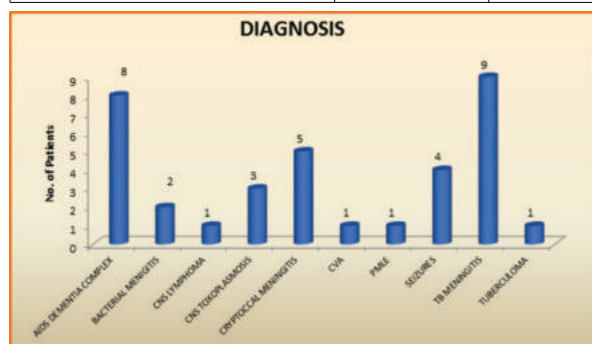


Chart No 8 Various Neurological Manifestations And Its Incidence

DISCUSSION

Clinical Presentation

Altered Sensorium

The University of California and San Francisco data revealed altered sensorium as a manifestation of secondary viral infection. This was the most typical presenting symptom in the study. 8 out of the 35 patients

had altered sensorium (22.2%). As observed in this study, altered sensorium was mainly due to tuberculous meningitis being the most common cause, followed by cryptococcal meningitis, then tuberculoma, pyogenic meningitis and CNS Lymphoma. Progressive multifocal leukoencephalopathy, toxoplasmosis, cryptococcosis and H.I.V. dementia were the other causes.

Headache

20 patients with neurological symptoms presented with headaches (55.6%). Sixteen patients (80%) had opportunistic infections like tuberculous meningitis, cryptococcosis, pyogenic meningitis, CNS. toxoplasmosis and CNS lymphoma as the cause. One patient had AIDS Dementia as the cause. Headache is a prevalent symptom in HIV. infection because of the frequency of intracranial disease and mass lesions. Kale et al.³⁰ has frequently described headaches as a common symptom.

According to the study done by Kale et al., One hundred seven patients (53.5%) reported headache symptoms, the large majority of which were consistent with characteristics of primary headache disorders after excluding 4 cases attributable to secondary causes; among those who met the criteria for a primary headache disorder, 88 (85.44%). Fifteen patients (14.56%) had the episodic or chronic tension-type headache criteria. The severity of H.I.V., which was based on the CD4 count but not the duration of H.I.V. or the number of prescribed antiretroviral medications, was more associated with headache severity, frequency, and disability and distinguished migraine from Tension-Type Headache.

Headache is of two types. One is the primary type, and the other is a secondary type of headache. Causes of primary headache were tension-type, cluster, depression or migraine cause. The secondary causes were primarily due to infections causes like TB meningitis, Bacterial meningitis, Cryptococcal meningitis, CNS Toxoplasmosis, CVA, AIDS Dementia Complex, Tuberculoma or PMLE.HIV encephalitis and dementia are common in the HIV patients. In comparison with Kate et al study and my study the incidence of occurrence of the disease was 53.5% and 55.6%.

Seizures

In our study, the common cause for seizures was neurotuberculosis. Of the 35 patients, four patients had seizures (11.4%). Two patients had regular MRIs. The brain showed multiple ring-enhancing lesions and showed leptomeningeal enhancement in the patients. CSF. analysis did not reveal any abnormality. EEG. in these patients showed bilateral epileptiform activity.This is perhaps because approximately half the HIV infected patients have no definite identifiable disease of the brain, and cerebral HIV. infection seems to be the likely cause of the seizures, as reported by Holtzman et al.⁷. the study had HIV encephalopathy as the cause of attacks in 24% of the patients. Seizure as an initial manifestation was rare in this. In most patients, the attack was a recent onset at admission. It started after current hospital admission (42.5%) or three months before entry (52.5%), indicating that most seizures were related to neurological complications due to HIV infection. The most common reasons of seizure were found to be cerebral toxoplasmosis (46%), tuberculous meningitis (35.6%), and cryptococcal meningitis (13.7%), which is similar to most other studies Toxic-metabolic (59%) and HIV encephalopathy (22%) were the most typical causes of seizure in other studies, respectively. HIV encephalopathy is a common cause of attacks in developed countries. This may be partly because early and effective treatment of H.I.V. infection is complex in developing countries. Hence, HIV-infected patients have a higher incidence of CNS. opportunistic infections. In comparison with Holtzman et al study and my study the incidence of occurrence of the seizures was 24% and 11.1%.

Paraparesis

One patient had paraparesis on presentation in our study (2.8%). It was due to C.V.A. The other causes affecting were Human T cell lymphotropic virus 1, tuberculosis, herpes zoster, and syphilis were the causes of paraparesis described by A. I Bhigjee et al.³. in their study. In comparison with A.I Bhigjee et al study and my study the incidence of occurrence of paraparesis was 2% and 2.8%.

Praesthesias

Two patients in our study had paraesthesias of both lower limbs (2.8%). An electrodiagnostic study done in these two patients showed slowing of sensory conduction of lower limb sensory nerves. Both the patients were on antiretroviral therapy (which included zidovudine)

and improved with amitriptyline and nutritional support. In comparison with Holtzman et al⁷ study and my study the incidence of occurrence of the paresthesia was 21%, 8.82% and 2.8%.

Aids Dementia Complex

Among the 35 patients, eight have AIDS dementia complex (22.9%). The patient presented with headaches and progressive cognitive decline. The Mini-mental score of the patient was 24. CT brain and CSF analysis was normal. Impaired memory and concentration with psychomotor slowing represent the early joint presentation of this disorder. Bandyopadhyay et al.⁵ reported 21% incidence in their studies, respectively. Because of these findings, baseline MMSE is probably advisable for all cases with HIV seropositivity, and periodic evaluation may unearth more possibilities with the AIDS dementia complex. The features are divided into three areas, namely cognitive deficits, behaviour changes and motor symptoms. Prominent features of H.A.D. They included substantial memory deficits, loss of executive function, poor attention and concentration. Behavioural changes in H.A.D. are commonly like apathy, and lack of motivation (abulia) was expected. Patients had displayed irritation, reduction in weight, restlessness, and increased anxiety. Motor symptoms and signs — like difficulty in movement of limbs, dysidiadochokinesia, hyperreflexia, and frontal release signs such as grasp, root, snout, and glabellar reflexes were present. In comparison with Bandyopadhyay et al study and my study the incidence of occurrence of the AIDS DEMENTIA COMPLEX was 21% and 22.9%.

Neurotuberculosis

10 out of 35 patients who had neurological symptoms had a tuberculous nervous system infection in our study. Among the ten patients, 9 had tuberculous meningitis (25.7%), and 1 had tuberculoma (2.9%). Eight among the nine patients who had tuberculous meningitis had expired (88.88%). Majority of them had headaches, then altered sensorium, and seizures to the patient.

The number of tuberculosis cases in India is very high. The patient diagnosed with tuberculoma presented with headache with altered sensorium M.R.I. brain had revealed multiple ring-enhancing lesions. C.S.F. analysis was elevated protein, with most of them constituting the lymphocytes. Once the patient becomes immunodeficient, there is the bacillus reactivation, resulting in T.B. meningitis. Many patients' had tuberculous meningitis was the first manifestation of the disease, and many were not on retroviral therapy. They had headache, fever and vomiting. They may have altered sensorium, personality changes and coma. Presence of cranial nerve palsies are common in the patients. The most common cranial nerve to be affected is the sixth one and the second that is the optic nerve. Some patients might be having only cranial nerve palsies and were later found to be having meningitis. It has three phases prodromal phase, meningitic phase and paralytic phase. Some patients will present with loss of memory, dementia and loss of libido and convulsions without overt signs of meningitis. In comparison between William P et al study, Mara S et al and my study the incidence of occurrence of the tuberculosis was 50%, 57% and 25.7%.

Pyogenic Meningitis

Two patients had features of pyogenic meningitis (6.25%)—both the patients presented with altered sensorium, fever and headache. C.T. brain was average, and C.S.F. analysis revealed elevated proteins and predominant neutrophils in cytology. C.S.F. culture was showing one organism. However, both the patients had the disease, proving that pyogenic infection coexisting with H.I.V. infection has a very high mortality. Studies from third world countries, such as Baingana et al.⁶ from Uganda, reported a 7% incidence of bacterial meningitis. The most common etiologic agent was acute bacterial meningitis is the *Streptococcus pneumoniae* in AIDS patients in our which is according to the other studies^{6,7} In comparison with Baingana et al study and my study the incidence of occurrence of the disease was 7% and 5.7%.

Cryptococcal Meningitis

Of the 32 patients, one had cryptococcal meningitis (3.13%). Headache, altered sensorium and signs of meningeal irritation were the presentation. CSF analysis in this patient was positive for *Cryptococcus* on India ink preparation. In comparison with Bandyopadhyay et al study and my study the incidence of occurrence of the disease was 3.7% and 3.13%.

Progressive Multifocal Leukoencephalopathy

One patient in our study was diagnosed with progressive multifocal leukoencephalopathy (3.13%). The Mini-mental score of the patient was 14. CSF analysis showed no abnormalities. MRI brain revealed extensive white matter lesions which had involved the left caudate nucleus, capsuloganglionic region, and bilateral parietal and occipital regions, enhancing the T2W flair image.

Snider et al.¹ studied 50 patients with AIDS, in which he had two patients with progressive multifocal leukoencephalopathy. In comparison with Snider et al study, S K Sharma et al, my study the incidence of occurrence of the disease was 4%, 1.2% and 3.13%.

Cerebrovascular Accident

One patient in our study presented with cerebrovascular complications (2.8%). The patients presented with hemiparesis, and their MRI brain showed a middle cerebral arterial territory infarct. The patient had a poor GCS(6/15). On admission and he expired on the same day. Gupta et al¹ has reported 8.82% incidence of CVA in seropositive patients in his study.

In the study as described by Chow et al.⁸ 0.5% incidence of CVA in seropositive patients. HIV infection is also an independent risk factor for developing stroke. There are several causes of stroke in patients with H.I.V. infection. There are different incidents of stroke based on the age of the patient. In general, studies from Asia had yielded a lesser incidence of the cases. Chow et al.⁸ had reported that the incidence rate of ischemic stroke per 1000 person-years was almost 5.27 in the HIV cohort and 3.75 in patients without HIV, and the incidence of hemorrhage stroke per 1000 person-years was found to be 2.29 in the HIV-infected group compared with 1.23 in non-HIV group 52 in a local U.S. health care system. Few studies have reported the association between HIV infection and risk of stroke by age and sex. Our observation was based on the finding of Chow et al.⁸, which had demonstrated a higher H.I.V. infection-related risk of ischemic stroke in young people. In comparison between Chow et al study, Gupta et al study and my study the incidence of occurrence of the CVA was 0.52% ,8.82% and 2.9%.

CONCLUSION

The incidence of neurological manifestations was around 35% in our study Headache and altered sensorium were the two common symptoms observed in this study. Most of the patients in our study had a heterosexual transmission of disease. Neurological manifestations in men are more common than in women. Meningitis caused by tubercle bacilli was the most common disease in this study group, and the next was the cryptococcal meningitis. Many of the patients who had the disease were of young age Many of the patients had expired No significant CD4 count correlation was found between the patients with neurological manifestations and those without neurological manifestations. Patients with neurological manifestations had high mortality and poor outcome. Tuberculous and pyogenic meningitis were associated with very high mortality. CD4 count of low had increased mortality. Patients with coexisting tuberculous meningitis and HIV had significantly lower CD4 counts. Of the 100 patients, 35 had neurological manifestations.

REFERENCES

- 1) Gupta SS et al. Neurological manifestations of HH.I.V.-1 infection and AIDS. *CARC Calling* 1993;6:30-32
- 2) Kirkland, K. E., Kirkland, K., Many, W. J., Jr, & Smitherman, T. A. (2012). Headache among patients with HIV disease: prevalence, characteristics, and associations. *Headache*, 52(3), 455–466.
- 3) A.I.Bhigjee MD, S.Madurai Msc, P.L.A.Bill FRCP, et al. Spectrum of myelopathies in HH.I.V.seropositive South African patients. *Neurology* 2001;57:348-351.
- 4) Luma, H. N., Tchaleu, B. C., Doualla, M. S., Temfack, E., Sopouassi, V. N., Mapoure, Y. N., & Djientcheu, V. D. (2012). HIV-associated sensory neuropathy in HIV-1 infected patients at the Douala General Hospital in Cameroon: a cross-sectional study. *AIDS research and therapy*, 9(1), 35.
- 5) Bandyopadhyay D, Sarkar RN, Mandal SK, Bandyopadhyay R. Neurological manifestations of HIV/AIDS. *JAPI* 2005;53:379.
- 6) Baingana et al. Neurological disease in Uganda AIDS patients. *International Conference on AIDS* 1991;7:187
- 7) S o YT, Holtzman DM, Abrams DJ, et al. Peripheral neuropathy associated with acquired immunodeficiency syndrome: Prevalence and clinical features from a population – based survey. *Arch Neurol* 1988;45
- 8) Chow, Felicia C. MD; Regan, Susan PhD; Feske, Steven MD; Meigs, James B. MD, MPH; Grinspoon, Steven K. MD; Triant, Virginia A. MD, MPH. Comparison of Ischemic Stroke Incidence in HIV-Infected and Non-HIV-Infected Patients in a US Health Care System. *JAIDS Journal of Acquired Immune Deficiency Syndromes*: August 1, 2012 - Volume 60 - Issue 4 - p 351-358
- 9) Sharma, S. K., Soneja, M., Ranjan, S., Miglani, S., Hari, S., Sinha, S., & Wig, N. (2013). Progressive multifocal leukoencephalopathy in HIV/AIDS: observational study from a tertiary care centre in northern India. *The Indian journal of medical research*, 138(1), 72–77.