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Original Article

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Study of Neurological and Biochemical Manifestations in HIV Patients

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Abstract

***Background & Aims*:** Nervous system involvement causes significant degree of morbidity in the patients with Human Immunodeficiency Virus (HIV) infection. At least 10% of the cases of Acquired Immune Deficiency Syndrome (AIDS) present with neurological symptoms and over the course of the illness symptomatic involvement of the central and peripheral nervous system has been found in 30 to 60% of the patients.

***Materials & Methods*:** This study included the patients with HIV disease presenting various neurological manifestations admitted into Departments of Medicine and Neurology. In all cases provisional diagnosis was made by taking detailed history and clinical examination. All the cases were subjected to investigations like CD4 count, CSF analysis, EEG, nerve conduction studies, and CT scan and MRI of brain and spinal cord to establish the etiology.

***Results*:** The predominant symptoms observed in the study were headache (70%) and fever (65%). Out of the 100 patients, 30 patients presented with seizures. Central nervous system tuberculosis is the underlying cause in 50% of the cases. Neck stiffness and positive kernig's sign were seen in 55%. CSF analysis of the patients disclosed a picture suggestive of tuberculosis meningitis in 60%. The radiological evaluation in the form of CT or MRI brain showed lesions like cortical infarcts in 28%.

***Conclusion*:** The study disclosed tuberculosis of the CNS to be the major cause for seizures and other neurological disorders in HIV. Even though neurological manifestations can occur at any level of CD4 count, prognosis is bad if CD4 count is less than 200.

***Keywords*:** HIV, CNS Manifestations, CSF Analysis, Neuroimaging Studies

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Introduction

Nervous system involvement causes significant degree of morbidity in the patients with HIV infection. At least, 10% of cases of AIDS present with neurological symptoms and over the course of the illness symptomatic involvement of the central and peripheral nervous system has been found in 30 to 60% of the patients (1). Immune mediated disorders with

neurological consequences may occur during the course of HIV infection as the body immune system becomes dysfunctional (2). Once the immune system is no longer capable of effectively defending, the nervous system also becomes vulnerable to opportunistic infections, neoplasms, and encephalopathy (3). After the introduction of Highly Active Antiretroviral Therapy (HAART) in 1996, the neurological manifestations of HIV-1 infection did not decline like the other complications of immunodeficiency; in contrast, due to increased longevity of HAART treated HIV-1 positive individuals, prevalence of virus associated neurological disease like aseptic meningitis, HIV encephalopathy, etc., increased during the last years, as international studies underline (4). Therefore, clinicians and HIV therapists should be able to diagnose HIV-1-associated neurological diseases even in their early stages. Although extensive studies on HIV/AIDS have been done in the West, there is a pressing need for elaborate study in our locality owing to the difference in social, economic, cultural, and educational backgrounds (5, 6). Studies need to define clinical aspects, early recognition, spread, natural course, and effective disease control. The present study was conducted to find out such aspects of HIV/AIDS with nervous system involvement.

Materials & Methods

This study included 100 patients with HIV disease presenting with various neurological manifestations that were admitted into the Departments of Medicine and Neurology over a period of 2 years. Patients below 13 years were excluded from the study. In all cases provisional diagnosis was made by taking detailed history and clinical examinations. All the cases were subjected to relevant investigations like CD4 count, serological investigations, CSF analysis, EEG, nerve conduction studies, and radio imaging modalities CT scan and MRI of brain and spinal cord, where it was needed to establish the etiology of the disorder. All the cases were followed up regularly throughout their hospital stay and subsequently after discharge.

Results

100 cases of established HIV infection with various neurological manifestations who were admitted to medical and neurology wards were evaluated.

Sex incidence:

Males were predominantly affected (Table 1).

Table 1. Sex distribution among the studied Patients

Male	75
Female	25

Age incidence:

None were observed below 20 years of age. The majority of patients in the study were young adults who belong to reproductive age group (Table 2).

Table 2. Age distribution among the studied Patients

Age Group	No. of Patients
20-30	32
30-40	48
40-50	13
50-60	5
60-70	2

Analysis of symptoms:

The predominant symptoms observed in the study were headache (70%) and fever (65%) (Table 3).

Table 3. Predominant symptoms observed in the study

Symptoms	Frequency	
	No. of patients	Percentage
Headache	70	70%
Fever	65	65%
Altered Sensorium	40	40%

Irritability	40	40%
Behavioural abnormality	25	25%
Focal deficit	30	30%
Seizures	30	30%
Vomitings	35	35%
Sensory Abnormality	15	15%
Diplopia	10	10%
Unsteadiness	12	12%
Lethargy	10	10%
Loss of Consciousness	8	8%
Loss of weight	25	25%

Types of seizures:

Out of the 100 patients 30 patients presented with seizures. Majority of them presented with generalized Tonic-Clonic seizures (66.6%) (Table 4).

Table 4. Types of seizures in the study

Types of Seizure	No. of patients	Percentage
Generalized Tonic-Clonic Seizure	20	66.6%
Simple partial seizure	6	20%
Status epilepticus	4	13.4%

Underlying cause:

Central nervous system tuberculosis is the underlying cause in 50% cases (Table 5).

Table 5. Underlying causes of AIDS

Underlying cause	No. of patients	Percentage
CNS Tuberculosis	15	50%
Cryptococcal Meningitis	5	16.6%
Toxoplasmosis	4	13.4%
Progressive multi focal leucoencephalopathy	2	6.6%
AIDS Dementia	1	3.3%
Cysticercosis	1	3.3%
Cerebral malaria	1	3.3%
Metabolic	1	3.3%

EEG Abnormalities:

Out of 30 cases presenting with seizures, EEG showed abnormality in 18 cases and normal in 12 cases (Table 6).

Table 6. EEG Abnormalities in the study

EEG	No. of patients
Normal EEG	12
Regional Slowing and Epileptiform discharges	2
Regional slowing	9
Generalized and diffuse slowing	7

Analysis of signs:

Among the various clinical signs meningeal irritation in the form of neck stiffness and positive kernig's sign were seen in majority of cases (55%) (Table 7).

Table 7. Analysis of signs in the study

Clinical Signs	**Frequency**	
	No. of patients	**Percentage**
Meningial irritation	55	55%
Hemiplegia	25	25%
Cranial neuropathy	12	12%
Memory disturbances	15	15%
Paraplegia	6	6%
Quadriplegia	2	2%
Peripheral Nerve Involvement	5	5%

CSF analysis:

CSF analysis of the patients disclosed a picture suggestive of tuberculosis meningitis in 60% of cases (Table 8).

Table 8. CSF analysis of the studied patients

CSF ANALYSIS	**PERCENTAGE**	**NEUTROPHILS (X 10^6/L)**	**LYMPHOCYTES (X 10^6/L)**	**GLUCOSE (mg/dL)**	**PROTEIN (g/dL)**
TB meningitis	60%	5(0-23)	64 (18-140)	26(16-45)	2.1(1.1-3.6)
Cryptococcal meningitis	11%	0 (0-4)	19 (10-63)	39 (26-54)	1.0 (0.6-1.8)
Aseptic meningitis	4%	0 (0-2)	7 (2-11)	63 (46-70)	0.7 (0.3-1.1)
Normal	25%	0 (0-0)	1 (0-4)	74 (40-74)	1.7 (1.2-2.7)

Brain CT Scan and MRI:

The radiological evaluation in the form of brain CT scan or MRI showed majority lesions like cortical infarcts in 28%. Normal scan of brain was noticed in 35% of the cases.

Table 9. Brain CT Scan and MRI in the study

CT Scan & MRI Brain	Percentage
Cortical infarct	28%
Tuberculoma	15%
Toxoplasmosis	7%
Hydrocephalus	6%
Progressive Multifocal leucoencephalopathy	3%
Lymphoma	2%
Cerebral atrophy	6%
Cerebellar Infarct	2%
Cysticercosis	1%
Normal scan	35%

Common Neurological disorders and their mean CD4 count:

CD4 count was done in 76% of the cases. CD4 counts could not be done in rest of the cases as they presented in very advanced stages of the disease and died before CD4 count could be done (Table 10).

Table 10. Common Neurological disorders and their mean CD4 count in the study

Neurological Disorders	Mean CD4 count
Tuberculousis Meningitis	126
Toxoplasmosis	135
Cryptococcal Meningitis	80
Aseptic Meningitis	230
HIV Encephalopathy	160

Out Come: out of 100 the patients, 28 patients died and 72 cases survived.

Discussion

The study of various neurological disorders of HIV/AIDS had been undertaken to evaluate the etiology, various neurological manifestations and their outcome.

The age group of the patients mostly involved in the present study was in the range of 20-40 years (80%), and it was in correlation with other studies like study of Wadia et al. (85-90%) (7). Males were predominantly affected (75%) compared to females which can be compared to the studies like study of Lanjewar et al. (80%) and Gongora-Rivera who reported 89% male involvement (8, 9). Agricultural labourers and lorry drivers mostly comprise this group and their occupation involves travel to distant places and exposure to multiple partners. Poverty, illiteracy, and cheap recreation prevalent in these parts also predispose young males to HIV infection. Females constituted 25% of the cases.

Headache (70%) and fever (65%) were two major presenting features pointing towards the increased frequency of opportunistic infections (Table 3). Meningeal irritation was present in 55% of the patients. Tuberculous meningitis constituted the major neurological presentation (60%) in our study, which can be compared with the studies like study of Simpson et al., Singh et al., and G. Modi et al. (46%) which reported Tuberculous meningitis as the most common neurological manifestation in HIV (10-12).

Seizures are a relevant neurological symptom during the course of HIV infection. There are 30 cases (30%) out of 100 cases presented with seizures which could be correlated with other studies like Sinha et al. where the

incidence was about 20% (13). Higher incidence of seizures was noted in the present study compared to the results of Chadha et al. which reported 5% (14). This could be due to increased involvement of the nervous system by tuberculosis in its various forms in the patients with HIV infection and moreover, the present study included patients who had neurological illness but the study of Chadha et al. included HIV seropositive patients with either neurological or non-neurological illnesses.

Behavioral abnormalities and cognition impairment were seen in 25% of the patients. However cognitive impairment and behavioral abnormalities were reported only in 10% of the cases by Wadia et al. (7). This variability could be explained as factors like socioeconomic status, education, and coexistent malnutrition influence the behavior and cognition in a particular study.

Sensory abnormalities were found in 15% of the patients in the present study, which was in accordance with the study of Gongora-Rivera et al. (19.4%) (9). The sensory abnormalities were predominantly objective, which were detected by careful neurological examination in the form of peripheral neuropathy. Subjective paresthesia was also noted in some patients. Cranial neuropathy was significantly higher in this study (12%) compared to the study of Wadia et al. who reported 2.9% (7). This may be due to the increased severity of vasculitis secondary to meningitis.

CSF analysis showed a picture of tuberculous meningitis in 60% of the patients. The CSF in these patients showed a lesser raise in CSF cell count of chronic inflammatory cells, probably due to a suppressed cell mediated immunity and inability to elicit a reaction to infection. Cysticercosis was diagnosed in one patient who was not reported in any of the previous studies. The high prevalence of cysticercosis in the community and faulty food habits might have predisposed this patient to cysticercosis.

Patients with tuberculosis of CNS showed an aggressive form of disease with a higher incidence of radiological lesions and focal neurological deficits. The incidence of stroke was very high in our study i.e., 25% in comparison to 5.6% in Wadia et al. study (7). The increased trend towards basal vasculitis in both tuberculous meningitis and other causes of meningeal infection might explain the higher incidence in our study.

CNS toxoplasmosis was detected in 7% of the patients in whom CT scan brain was done. This was correlating with the studies of Wadia et al. (8.5%) (7) and Rachilis et al. (2-10%) (15). These results do not correlate with the Western studies which had toxoplasmosis as the most common radiological lesion (3-5), while in our scenario it was tuberculous meningitis which manifests either as infarct or tuberculoma. The widespread use of Co-Trimoxazole for the treatment of Pneumocystis jiroveci and other infections which usually coexist with HIV infection might have kept a check on the occurrence of Toxoplasmosis infection in our area.

The incidence of myelopathy in our study was 3% and correlates with the study by Wadia et al. 4.8% (7). Neuropathies including Herpes zoster, peripheral neuropathy, radiculopathy, and cranial neuropathy were 17% in our study which was comparable with 28% in the study of Wadia et al.

The study showed a low incidence of cryptococcal meningitis (11%) and similar pattern was seen in other studies like Chadha et al. (14.7%). The study by Frimpong could not detect even a single case of HIV with cryptococcal meningitis, indicating difference in prevalence of cryptococcal meningitis in different areas (16). On the other hand, the incidence of cryptococcal meningitis was reported to be very high in the Western studies (3-5).

HIV encephalopathy was observed in 2% of the study group, which was less than Wadia et al. (7) and Rachilis et al. (15) studies (6.7%), and the K.Kothari study 13% (17). Increasing the number of patients in the study group over an extended period of time and follow-up of these patients might increase the yield of HIV encephalopathy (17). This would explain the less number of HIV encephalopathy detected in our study compared to the western scenario.

Malaria is endemic in our area and P. falciparum is commonly associated with cerebral malaria. HIV patients with super infection by this agent would have a downhill course of the disease due to complicated cerebral malaria which was observed in 2% of the patients in our study.

CNS lymphoma was seen in 2% of the study group and is in comparison with 1.3% in Gongora-Rivera et al. study (9) and 5% in Rachilis et al. study (15). The lack of brain biopsy facilities and limited resources for histopathological examination were the cause for lower incidence of CNS lymphoma in our study.

Conclusions

In summary, the study disclosed tuberculosis of the CNS to be the major cause for seizures and other neurological disorders in HIV. It manifests mostly as an uncomplicated tuberculous meningitis. Probably the high incidence of CNS preponderance by tuberculosis could be due to increasing prevalence and the chronicity of the disease in HIV-affected communities. Even though neurological manifestations can occur at any level of CD4 count, prognosis is bad if CD4 count is less than 200.

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No Declared

Conflict of interest

No conflict of interest declaration between the authors.

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Ethical statement

This study was approved by the institutional review board and followed the ethical principles of the Declaration of Helsinki. All patients with HIV disease who participated in the study gave their informed consent after being informed about the purpose, methods, and potential risks and benefits of the study. The confidentiality and privacy of the patients were protected throughout the study and the data analysis.

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