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Neuropsychiatric Manifestations in HIV Patients: A Hospital Based Study

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ABSTRACT

Acquired Immunodeficiency Syndrome (AIDS) has manifested as a complex array of diseases since its recognition in 1981. Neurological and neuropsychiatric complications are emerging as significant challenges within this landscape. This study aimed to comprehensively explore neuropsychiatric manifestations in HIV-positive patients, their associations with CD4 T cell counts and the influence of opportunistic infections. A prospective, one-year study was conducted at a medical institution in collaboration with the department of psychiatry. HIV-positive patients admitted between September 2006 and August 2007 were included. Comprehensive clinical assessments, psychiatric rating scales, serological screenings, opportunistic infection evaluations, CD4 cell counts and radiological investigations were conducted. Statistical analyses were employed to discern patterns and correlations. The study group comprised 100 HIV-positive patients, primarily aged 31-35 years (35%), with a male-to-female ratio of 9:11. Unprotected heterosexual contact, particularly with professional sex workers, was the primary mode of transmission. Tuberculosis (51.6%) and oral candidiasis (25%) were predominant opportunistic infections. Neurological complaints were observed in 47% of patients, most commonly altered sensorium (70.21%), with underlying causes such as tubercular and cryptococcal meningitis. Psychiatric manifestations were significant, encompassing anxiety (57.7%), depression (23%), cognitive dysfunction (11.6%) and dementia (7.7%). A strong correlation was observed between CD4 T cell counts and neuropsychiatric symptoms, with anxiety and depression linked to higher counts and cognitive impairment and dementia to lower counts. This study underscores the complex and diverse neuropsychiatric manifestations in HIV-positive patients, emphasizing the role of immunosuppression and opportunistic infections. Understanding the intricate interplay between HIV infection, CD4 T cell counts and neuropsychiatric outcomes is vital for effective management and improved quality of life. Timely interventions addressing both CNS and psychiatric aspects can enhance the overall well-being of individuals living with HIV.

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) emerged onto the global medical landscape in 1981, marked by the perplexing clustering of uncommon diseases such as Pneumocystis carinii Pneumonia among young homosexual men in Los Angeles and New York. Soon, the spectrum of AIDS cases expanded to encompass diverse populations including intravenous drug users and hemophiliacs[1-3].

Characterized by a profound breakdown of the immune system, AIDS is aptly termed a syndrome due to its manifestation as a collection of diseases that render the chost susceptible to severe and often fatal infections, opportunistic infections and certain malignancies. Despite robust immune responses, HIV establishes a chronic infection characterized by the gradual decline of CD4 T cells, opening the door to a multitude of clinical manifestations across respiratory, gastrointestinal, hematological and neurological systems, particularly evident in the setting of advanced HIV infection[3,4].

Among the significant challenges posed by AIDS, neurological and neuropsychiatric complications have garnered increasing attention. The spectrum of neuropsychiatric and neurological manifestations in HIV/AIDS is extensive and multifaceted. These manifestations encompass a range of symptoms, including progressive dementia, depression, psychomotor slowing and psychiatric presentations like manic symptoms and atypical psychoses. The prevalence of clinical neurological abnormalities among AIDS patients is estimated at 40-70%, with neuropathological changes present in 75% of cases upon autopsy. Various factors contribute to these manifestations, including the direct impact of HIV-1 on nervous tissue, secondary opportunistic infections, tumors, cerebrovascular disease and complications from systemic AIDS treatments. Additionally, HIV-associated neuropathy and related conditions, such as Guillain-Barre Syndrome, have been reported. The advent of antiretroviral therapy has reshaped the landscape of AIDS-related neurological complications, highlighting the need for vigilant assessment and management strategies[5-8].

Aims and objectives:

The primary aim of this study is to comprehensively investigate the diverse neuropsychiatric manifestations in HIV-positive patients, thereby enhancing our understanding of the intricate interplay between HIV infection and the central nervous system. The study will elucidate the association of CD4 T-cell counts with various neuropsychiatric abnormalities, shedding light on the correlation between immune status and neurological complications.

Specific objectives:

- To conduct a thorough assessment of presenting and neuropsychiatric manifestations in HIV-positive patients, encompassing cognitive deficits, psychiatric abnormalities, and motor disturbances
- To investigate the relationship between CD4 T cell counts and the prevalence and severity of neuropsychiatric abnormalities in HIV-positive individuals
- To explore the impact of various opportunistic infections on the neurological status of HIV-positive patients, contributing to the understanding of the complex interactions between HIV infection and associated complications

MATERIALS AND METHODS

Study design: This prospective study was conducted over a one-year period, from September 2006 to August 2007, at the Department of Medicine in collaboration with the Department of Psychiatry at Indira Gandhi Medical College and Hospital, Shimla.

Patient selection

Inclusion criteria: All HIV-positive patients admitted to I.G.M.C. hospital, Shimla, between September 2006 and August 2007, in the Departments of Medicine and Psychiatry.

Exclusion criteria: Patients with a history or physical examination suggesting neurological and psychiatric disorders prior to HIV diagnosis and Patients with diabetes.

Patient consent: Informed consent was obtained from all participants in the study. Consent for HIV testing was obtained before collecting blood samples.

Clinical assessment: Patients were clinically evaluated following relevant medical history and comprehensive general and systemic examinations. Specific investigations were conducted to establish diagnoses and screen for opportunistic infections. Psychiatric rating scales were administered to assess mental health and further assessments including CT scans, MRI brain scans and CSF examinations were conducted as necessary to evaluate neuropsychiatric dysfunction.

Diagnosis establishment

Serological screening: Venous blood samples were collected aseptically and ELISA tests for HIV were performed using commercially available kits. (Genedia ELISA for HIV, ACON RAPID CARD and COMB AIDS.

Screening for opportunistic infections (OI):

- **Respiratory pathogens:** Sputum examination was conducted by having patients cough directly into sterile containers. Gram's smear and culture were used to detect bacterial and fungal infections

- **Gastrointestinal tract (GIT) infections:**
  - Stool samples were examined for ova, cysts, and parasites
  - Gram's stain and culture on sabourd's dextrose agar (SDA) were used to identify fungal infections

Central nervous system (CNS) infections: CSF examination included tests for protein, cytology, CSF sugar and concomitant blood sugar. Specific tests for Cryptococcus neoformans and bacterial meningitis were conducted and CSF culture was performed.

Skin and mouth infections: Gram's smear and culture were used to detect fungal infections in skin scrapings and buccal specimens.

CD4 cell count: CD4 cell counts were determined using a fluorescent activated cell sorter system.

Radiological investigations: CT and MRI scans were conducted when indicated based on clinical assessment.

Psychiatric evaluation:

- **Depression:** Depression assessment utilized the hamilton rating scale for depression (HAM-D, HRSD)
- **Anxiety:** Anxiety assessment used the hamilton rating scale for anxiety (HAM-A)
- **Cognitive dysfunction:** Cognitive status was evaluated using the general practitioner cognitive assessment tool, trail making test and mini mental state examination
- **Mania:** Manic symptoms were assessed using the young mania rating scale (YMRS)
- **Psychosis:** Psychosis assessment utilized the scale for positive symptoms (SAPS) and the scale for negative symptoms (SANS)
- **Dementia:** Dementia assessment involved the mini mental state examination (MMSE), general practitioner cognitive assessment tool (GPCOG), and dementia rating scale

Ethical considerations: The study was conducted following ethical guidelines, and informed consent was obtained from all participants. The study's protocol was approved by the appropriate ethical review board.

Data analysis: Collected data were analyzed using appropriate statistical methods to identify patterns, correlations, and associations among variables. The significance of differences was determined using statistical tests and the results were interpreted to draw meaningful conclusions.

RESULTS

One year prospective study from 1" July 2006 to 30 June 2007 was conducted in the Department of Medicine in collaboration with the Departments of Psychiatry at IGMC, Shimla. The study group included 100 patients with HIV infection admitted in various departments of IGMC Shimla fulfilling inclusion criteria.

Table 1 provides information about the demographic characteristics of the participants in the study. The participants were categorized based on age groups, gender, districts, professions and educational qualifications. The age distribution of patients ranged from 21-40 years. The highest number of patients (35%) fell within the age group of 31-35 years, followed by 30% in the 26-30 years age group. The study included 45% male patients and 55% female patients, resulting in a male-to-female ratio of 9:11.Among the districts represented, Hamirpur had the most participants (30%), followed by Bilaspur (18%) and Kangra (13%).The professions of male patients varied, with 71.1% being truck or taxi drivers, 13.1% uniformed personnel, 8.9% businessmen, 4.4% shopkeepers, and 2.2% farmers. Among the female patients, 90.9% were housewives and 9.1% were engaged in other professions. Educational qualifications were diverse, with 69% of patients having under-matric education, 25% being matriculate, 5% graduates and 1% postgraduates.

Table 1: Socio-demographic distribution of study participants

	No.	Percentage
Age group (year)		
21-25	15	15
26-30	30	30
31-35	35	35
36-40	20	20
Gender		
Male	45	45
Female	55	55
District		
Mandi	10	10
Sirmour	04	04
Kullu	07	07
Solan	05	05
Una	05	05
Hamirpur	30	30
Shimla	08	08
Bilaspur	18	18
Kangra	13	13
Profession of male patients		
Drivers	32	71.1
Uniformed persons	06	13.1
Businessmen	4	8.9
Shopkeepers	2	4.4
Farmers	1	2.2
Profession of female patients		
Housewife	50	90.9
Other	5	9.1
Educational qualification		
Undermatric	69	69
Matriculate	25	25
Graduate	5	5
Post graduate	1	1

Table 2: Presenting and neurological symptoms among study participants

Symptoms	No.	Percentage
Presenting symptoms		
Fever	44	44
Weight loss	38	38
Cough	17	17
Neurological complaints	47	47
Diarrhea	10	10
Genital ulcer	2	2
Neurological symptoms at presentation (n = 47)		
Altered sensorium	33	70.21
Headache	22	46.80
Gait instability	2	4.2
Memory impairment	2	4.2
Seizures	2	4.2
Focal neurological symptoms	2	4.2

Table 3: Clinical and neurological examination findings

Clinical examination	No.	Percentage
Pallor	44	44
Lymphadenopathy	18	18
Oral thrush	16	16
Consolidation	12	12
Hepatomegaly	11	11
Splenomegaly	8	8
Pleural effusion	6	6
Herpes simplex	4	4
Dementia	4	4
Ascites	2	2
Herpes zoster	2	2
Seborrheic dermatitis	2	2
Molluscum contagiosum	2	2
Scabies	2	2
Genital ulcer	2	2
Tineacruris	1	1
Neurological examination findings		
Altered sensorium	33	70.2
Features of meningeal	28	59.5
Focal neurological deficit	2	4.2
Ataxia	2	4.2
Bladder involvement	10	21.27
Peripheral neuropathy	4	8.5

Table 4: Biochemical and radiological findings

CD_4 counts	No.	Percentage
<50	26	26
51-100	32	32
101-150	15	15
151-200	16	16
201-250	16	16
>250	5	5
Abdominal ultrasonographic findings		
Hepatomegaly	11	11
Splenomegaly	8	8
Abdominal		
Lymphadenopathy	8	8
Hepatosplenomegaly	5	5
Ascites	2	2
Liver abscess	1	1
Normal study	66	66
Chest x-ray findings		
Consolidation	12	12
Pleural effusion	6	6
Milliary picture	3	3
Normal	79	79
CT head (plain) finding (n = 40)		
Diffuse cortical atrophy	13	32.5
Hypo dense area	2	5
Mass lesion	2	5
Normal	23	57.5
Various MRI abnormalities (n = 10)		
PML	2	20
Toxoplasmosis	3	30
Normal	5	50
CSF finding (n = 42)		
Tubercular	23	54.8
Cryptococcal	10	23.8
Normal 921.4		

Table-5: Various opportunisticiInfections

Various opportunistic infections	No.	Percentage
Tuberculosis	33	51.6
Candidiasis	16	25.0
Herpes Simplex	4	6.3
Cryptosporidium	2	3.1
Herpes zoster	2	3.1
Scabies dermatitis	2	3.1
Molluscum contagiosum	2	3.1
Genital ulcer	2	3.1
Tinea cruris	1	1.6
Total	64	100

Table 2 outlines the symptoms presented by the study participants upon admission and the associated neurological symptoms. Fever was the most common presenting symptom, observed in 44% of patients. Weight loss was reported by 38% of patients and cough was present in 17%. Neurological complaints were observed in 47% of patients, with altered sensorium being the most common neurological symptom (70.21%). Other symptoms included diarrhea (10%) and genital ulcers (2%).

Table 3 provides information about the clinical and neurological examination findings among the participants. Pallor (44%) and lymphadenopathy (18%) were common clinical findings. Oral thrush was present in 16% of patients and hepatomegaly was observed in 11%. Neurological findings included altered sensorium (70.2%), features of meningeal irritation (59.5%) and focal neurological deficits (4.2%).

Table 4 presents the results of biochemical and radiological investigations conducted on the study participants. Abdominal ultrasonographic findings revealed hepatomegaly (11%) and splenomegaly (8%), among other findings. Chest X-ray findings included consolidation (12%) and pleural effusion (6%). CT head (plain) findings showed diffuse cortical atrophy (32.5%) and hypo-dense areas (5%).Various MRI abnormalities were observed, such as PML (20%) and toxoplasmosis (30%). CSF examination indicated tubercular meningitis (54.8%) and cryptococcal meningitis (23.8%).

Table 5 lists the different opportunistic infections found among the participants. Tuberculosis was the most prevalent opportunistic infection (51.6%), followed by candidiasis (25%) and herpes simplex (6.3%). Other infections included cryptosporidium, herpes zoster, scabies, seborrheic dermatitis, genital ulcers, and tinea cruris.

Table 6 shows the gender distribution of neurological and psychiatric manifestations among the participants. Among neurological manifestations, altered sensorium (72.2%) was the most common, with various underlying causes, including tubercular meningitis and cryptococcal meningitis. Psychiatric manifestations included anxiety (57.7%), depression (23%), dementia (7.7%) and cognitive impairment (11.6%).

Table 6: Sex distribution in neurological and psychiatric manifestations

Neurological manifestations	Males	Females	Total
Neurological manifestation (total)	27	20	47
Tubercular meningitis	16	07	23
Cryptococcal	03	07	10
Toxoplasmosis	03	01	2
PML	2	0	2
Stroke	2	0	2
Cerebellar degeneration	1	1	2
Altered sensorium	20	13	4
Seizures	2	0	2
Psychiatric manifestations			
Psychiatric manifestations (total)	19	33	52
Depression	02	10	12
Anxiety	10	20	30
Dementia	03	1	4
Cognitive dysfunction	4	2	6

Table 7: CD4 count in patient with neurological manifestations

	Patients without CNS. abnormality	Patients with CNS. abnormality	p-value
No. of patients	52	48	
CD_4 count (Mean±S.D.)	116 ±95.89	61.68 ±34.16	<0.001
Range of CD_4 count	5-366	5-123	

Table 7 compares the CD4 cell counts of patients with and without neurological abnormalities. Patients with CNS abnormalities had a significantly lower mean CD4 count (61.68±34.16) compared to patients without CNS abnormalities (116±95.89). ($p<0.001$) The CD4 counts of patients with CNS abnormalities ranged from 5-123, while those without CNS abnormalities ranged from 5-366. Depression and anxiety were mainly seen with CD4 T cell count >150. Cognitive dysfunction was seen with CD4 count between 50-150 and dementia was mainly seen with CD4 counts 50.

DISCUSSIONS

The present study aimed to investigate the diverse neuropsychiatric manifestations of HIV infection and their potential correlation with CD4 T cell count. HIV infection is known to disproportionately affect young and economically productive sections of society. This progressive impairment of cellular immune functions leads to a decline in peripheral blood CD4 T lymphocyte levels, rendering individuals more susceptible to a wide array of opportunistic infections. The current research was designed to elucidate the different neuropsychiatric manifestations associated with HIV infection and their potential relationship with CD4 count.

Consistent with previous reports from the united States and Africa the study observed that the age group most affected was 31-35 years. Similarly, other studies by Idigbe *et al*.[9] in Elliott *et al*.[10] found the highest prevalence within the age group of 30-39 years. Chandra *et al*.[11] from Bangalore conducted a study in 1996 that also aligned with the age distribution observed in our study. This convergence of findings underscores the vulnerability of this particular age group to HIV infection.

The influence of professions such as driving and military service, along with patterns of travel and sexual behavior in a male-dominant society, resulted in a higher prevalence of HIV infection among males. This observation was consistent with the research by Adhikari[8] In contrast, our study showed a higher proportion of female patients, possibly due to males seeking treatment outside their region for professional or business reasons. Furthermore, female patients might have sought treatment only when their condition became severe, leading to a hospital-based bias.

Certain professions, including driving and military service, were associated with a higher susceptibility to HIV infection. Vishwanath *et al*.[12] found that drivers and businessmen constituted a significant portion of HIV-positive subjects. Similarly, our study showed that drivers accounted for a substantial portion of HIV-positive male patients. The pattern of uniformed personnel seeking care in military hospitals rather than government hospitals led to fewer instances in our study, consistent with findings by Adhakari[8]

The primary mode of HIV transmission was unprotected heterosexual encounters with professional sex workers, in line with various studies. Factors such as rural residence and separation from families due to work contributed to this high-risk behavior. Similarly, our study's subjects, mostly from rural areas, were more likely to engage in high-risk sexual behavior when away from their families. Additionally, all male patients in our study reported multiple unprotected sexual exposures with professional sex workers.

As the disease progressed, a decrease in CD4 T cell count led to increased susceptibility to opportunistic infections. Tuberculosis was identified as the most common opportunistic infection in our study, consistent with findings by Sincar *et al*.[13] and Kothari and Goyal[14]. Oral candidiasis ranked as the second most common opportunistic infection in our study, in line with findings by Vajpayee *et al*.[15]. Herpes zoster incidence also corresponded to similar studies.

The study delved into neuropsychiatric manifestations, which reportedly affect 40-73% of HIV-infected patients. CNS diseases encompassed infections like tubercular and cryptococcal meningitis, toxoplasmosis, and progressive multifocal leukoencephalopathy. Vascular complications and peripheral nervous system involvement were also observed. Psychiatric manifestations ranged from anxiety and depression to cognitive impairment and dementia.

Neuroimaging techniques, particularly MRI, played a crucial role in detecting CNS dysfunction. This was consistent with studies highlighting MRI's effectiveness in identifying HIV-related structural neuropathology. The present study found altered sensorium to be the most common neurological manifestation, followed by headache, seizures, ataxia and focal neurological deficits. Our findings aligned with studies by Chandra *et al*.[11] and Atilli *et al*.[16].

CD4 T cell count was found to correlate with neuropsychiatric symptoms. Anxiety and depression were associated with higher CD4 counts, while cognitive impairment and dementia were linked to lower counts. This observation echoed studies by Chandra *et al*.[11], Morrison *et al*.[17], Johnson *et al.*[18] and Alvarez *et al*.[19].

Comparative studies revealed variations in the prevalence of neuropsychiatric manifestations among HIV-infected individuals. These differences were attributed to factors such as demographics, disease stage and methodologies employed. It was evident that CNS involvement in HIV patients primarily arises from opportunistic infections at later stages of the disease, rather than direct pathogenic activity of HIV itself.

This study underscored the intricate neuropsychiatric manifestations of HIV infection and their potential link to CD4 T cell count. The findings were substantiated by a range of comparative studies and emphasized the multifaceted nature of neurological and psychiatric complications associated with HIV. Understanding these complexities is pivotal for delivering comprehensive care to individuals living with HIV.

CONCLUSION

The study concluded that younger individuals, particularly females, were more affected by HIV, often through unprotected heterosexual contact. Common symptoms included fever and weight loss, with Tuberculosis and oral candidiasis as frequent opportunistic infections. Neurological issues were observed in almost half of the patients, predominantly altered sensorium due to tubercular meningitis. Lower CD4 counts correlated with increased CNS and psychiatric manifestations, highlighting the impact of immunosuppression. Imaging and CSF analysis aided early detection of CNS involvement. Psychiatric disorders, especially anxiety and depression, were significant, more prevalent in females and linked to CD4 counts. The study underscores the need for timely management of CNS and psychiatric aspects to enhance the well-being and longevity of HIV-infected individuals.

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