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Clinical Profile of Neurological Manifestations Among HIV Positive Patients And Their Correlation with CD_4 Count

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Abstract:
Background & objectives: *Human immune deficiency virus (HIV) is a neurotropic virus which causes variety of neurologic manifestations either due to opportunistic infections and neoplasm or direct effects of HIV on nervous tissue. The objective of present study was to find out various neurological manifestations in HIV patients and their relation with CD_4 counts.*
Methods: *The present study included 200 symptomatic HIV patients attending ART center at tertiary care center of north India in the time period December 2012 to October 2014 were study. Out of which 57 patients were presented with neurological complications, all study subjects were thoroughly interviewed with detailed clinical history along with general physical examination, systemic examination and detailed neurological examination.*
Results: *Neurological complications were seen in 57 patients out of 200 and the commonest manifestation was tubercular meningitis in 47.37% patients followed by cryptococcal meningitis in 14%, HIV associated dementia in 8.80%, bacterial meningitis in 7%, progressive multifocal leucoencephalopathy in 5.30%, peripheral neuropathy in 5.30%, toxoplasmosis in 3.50%, cerebrovascular accident in 3.50%, cranial tuberculoma in 3.50% and acute inflammatory demyelinating polyneuropathy in 1.80% of HIV patients. 74.19% patients had CD_4 count <200/mm^3 and 22.81% had CD_4 count between 200-500/mm^3.*
Conclusion: *The prevelance of neurological manifestation in HIV patients was 28.50% and opportunistic infections were the leading cause of neurological disorder. Central nervous system infections, intracranial mass lesion, stroke and HIV associated dementia were more common in patients with a CD_4 count less than 200/mm^3.*
Key words: *HIV, Neurological Manifestation, Opportunistic infection, Neuropathy, Meningitis.*

I. Introduction

Human immunodeficiency virus is a lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome (AIDS) [1], a condition in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive.

HIV infects vital cells in the human immune system such as helper T cells (specifically $CD4^+$ T cells), macrophages and dendritic cells. HIV infection leads to low levels of $CD4^+$ T-cells through three main mechanisms: First, direct viral killing of infected cells; second, increased rates of apoptosis in infected cells; and third, killing of infected $CD4^+$ T cells by $CD8^+$ cytotoxic lymphocytes that recognize infected cells. When $CD4^+$ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections [2]. HIV is transmitted primarily by sexual contact (both heterosexual and male to male), by blood and blood products, and by infected mothers to infant intra-partum, perinatal, or via breast milk.

HIV-infected individuals can still experience a variety of neurologic abnormalities either due to opportunistic infections and neoplasms or to direct effects of HIV or its products. The main cell types that are infected in the brain in vivo are the perivascular macrophages and the microglial cells. A variety of monocyte-derived cytokines can contribute directly or indirectly to the neurotoxic effects in HIV infection; these include TNF-, IL-1, IL-6, TGF-, IFN-, platelet-activating factor, and endothelin [3].

Neurologic disease is the first manifestation of symptomatic HIV infection in roughly 10-20% of persons, while about 60% of patients with advanced HIV disease will have clinically evident neurologic dysfunction during the course of their illness [4,5].

II. Aims and Objectives

1. To study the clinical profile of various neurological manifestations in HIV positive patients.
2. To study the correlation between CD4 counts and the neurological manifestations.

III. Materials & Methods

Study comprised of cross sectional study design where 200 symptomatic HIV patients attending ART center at Government medical college, Patiala, Punjab in the time period December 2012 to October 2014 were studied. Subjects fulfilling the inclusion criteria, with age more than 15 years and positive for HIV by standard NACO guidelines were included in the study after written informed consent. Patients with history of other medical and neurological illness like diabetes, alcohol and other drug abuse like narcotics, sedatives and hypnotics, cerebrovascular accidents, epilepsy and Parkinsonism,

were excluded from the study. All study subjects were thoroughly interviewed with detailed clinical history along with general physical examination, systemic examination and detailed neurological examination including higher mental function, mini-mental state examination (MMSE), sensory, motor and cranial nerve examination. Despite of routine investigations, CD4 cell count, ELISA, nerve conduction study and cerebrospinal fluid (CSF) examination were done. All patients included in study were explained about the procedure, its purpose and were assured for confidentially of the information.

IV. Results

Present study included 200 HIV Positive patients, out of which 137 were male, 64 were female and 1 patient was male. Majority of patients were young to middle age group (26-45 year) and the mean age of HIV positive patients was 36.28±10.20 years. Most of HIV positive patients were married (170), laborer/farmer by occupation and most common mode of transmission was sexual transmission [table 1].

The neurological manifestations present in 57 patients in which most common neurological symptoms were altered sensorium (39), headache (30), convulsion (15), focal neurological deficit (15) [table 2].

Most HIV induced neurological illness due to opportunistic was tubercular meningitis (47.37%) followed by cryptococcal meningitis (14%), bacterial meningitis (4%) and primary illness were HIV associated dementia (5%), progressive multifocal leukoencephalopathy (3%), peripheral neuropathy (3%) [table 3].

In our study CD_4 count was done in 57 (28.5%) patients in which neurological manifestations present, in 44 patients CD_4 count was <200 and mean CD_4 count was 257.50±143.61 [table IV].

Mean CD_4 count was low in HIV induced neurological illness like Progressive multifocal leucoencephalopathy (63.66±13.05), Acute inflammatory demyelinating polyneuropathy (65), Toxoplasmosis (70±22.62) HIV associated dementia (92±31.63), Cryptococcal Meningitis (109±71.27), Bacterial meningitis (110.75±57.62), Peripheral neuropathy (159.33±40.21), Cranial tuberculoma (165±117.37), Tuberculous bacterial meningitis (181.44±83.50), Cerebrovascular accident (184±96.16) [table 4].

Table I: Distribution of patients according to sociodemographic profile

Variables	No. of patients (%) N=200
Age group	
16-25	30 (15%)
26-35	74 (37%)
36-45	67 (33.5%)
>45	29 (14.5%)
Mean age	
Gender	
Male	135 (67.5%)
Female	64 (32%)
Transgender	1 (0.5%)
Marital status	
Married	170 (85%)
Unmarred	30 (15%)
Mode of transmission	
Sexual	163 (81.5%)
Multiple	21 (10.5%)
Unknown	16 (8%)
Occupation	
Driver/conductor	48 (24%)
Laborer/farmer	72 (36%)
House wife	33 (16.5%)
Self employed	25 (12.5%)
Student	22 (11%)

Table II: Distribution of study subjects with Neurological symptoms

Neurological Symptoms	No. of patients (%) N=57
Altered Sensorium	39(68.42%)
Convulsions	15(26.32%)
Vertigo	03(5.26%)
FND	15(26.32%)

Cranial Nerve Abnormality	02(3.51%)
Sensory	03(5.26%)
Behavioural Abnormality	05(8.77%)
Headache	30(8.77%)

Table III: Distribution of study subjects based on Neurologic manifestations

Neurological illness	No. of patients (%) N=57
Acute inflammatory demyelinating polyneuropathy (AIDP)	1 (1.80%)
Bacterial meningitis (BM)	4 (7%)
Cryptococcal meningitis (CM)	8 (14%)
Cranial tuberculoma (CTBLM)	2 (3.5%)
Cerebrovascular accident (CVA)	2 (3.5%)
HIV associated dementia (HAD)	5 (8.80%)
Progressive multifocal leucoencephalopathy (PMLE)	3 (5.30%)
Peripheral neuropathy (PN)	3 (5.30%)
Tuberculous bacterial meningitis (TBM)	27 (47.37)
Toxoplasmosis	2 (3.50%)

Table IV: Distribution of study subjects based on CD4 count

CD4/ml	Frequency	Percentage	X^2/p
<200	44	77.19%	X^2=16.86
200-500	13	22.81%	
Mean	257.50±143.61		P=0.0001

Table V: Relation with CD4 count and neurologic illness.

Illness	Mean CD_4 cell count/mm^3
Tuberculous bacterial meningitis	181.44±83.50
Cryptococcal meningitis	97.25±71.27
Bacterial meningitis	110.75±57.62
Acute inflammatory demyelinating polyneuropathy	65
Peripheral neuropathy	159.33±40.21
Progressive multifocal leucoencephalopathy	63.66±13.05
Toxoplasmosis	70±22.62
Cerebrovascular accident	184±96.16
Cranial tuberculoma	165±117.37
HIV associated dementia	92±31.63
TOTAL	120.02±48.45

V. Discussion

In the present study, the age range of patients was from 16 to 62 years. Mean age was 36.28± 10.20 year. Majority of the patients were in the economically productive age group of 20-45 years [6,7,8]. Out of 200 patients 135 (67.5%) were male, 64 (32%) were female with a male to female ratio of 2.1:1 and 1(0.5%) patients was transgender. 85% of patient were married where as 15% were unmarried. Predominantly sexual transmission was observed in 81.5% of patients, multiple modes of transmission were present in 21 (10.5%) patients where as in 16 (8%) patients the exact mode of transmission could not be ascertained. Males have commonly acquired the disease through premarital and extramarital sexual contact, whereas females have mostly acquired the disease from their spouses. Females have generally been diagnosed as HIV positive during either routine antenatal check-ups or when their husbands came with opportunistic infections. In present study most of HIV patients was laborer/farmer by occupation 72 (36%) and 48 (24%) patients were driver/conductor, 33 (16.5%) were house wife, 25 (12.5%) were self employed and 22 (11%) were student [9,10].

In our study 200 patients were included out of which 57 patients had neurological involvement and the prevalence of neurological illness was 28.5%. Altered sensorium was the commonest neurological symptom seen in 39 (68.42%) patients, followed by headache in 30 (52.63%) patients, focal neurological deficit in 15 (26.32%) patients and convulsion in 15 (26.32%) patients of the patients [11,12].

In present study 27 (47.37%) patients had tubercular meningitis, 8(14%) had cryptococcal meningitis, 4 (7%) had bacterial meningitis, 5 (8.30%) patients had HIV associated dementia, 3 (5.30%) had PMLE, and 3 (5.30%) had peripheral neuropathy, 2(3.50%) patients were of each had intracranial tuberculoma, toxoplasmosis and CVA, 1 (1.80%) patient had acute inflammatory demyelinating polyneuropathy [13].

Among the 57 patients with neurological manifestation 44 (77.19%) had CD_4 <200/mm^3 and 13 (22.81%) had CD_4 count >200/mm^3. The mean CD_4 count was 257.50±143.61[14].

Mean CD_4 count was 181.44±83.50 in patients with TBM, 97.25±71.27 for cryptococcal meningitis, 110.75±57.62 for BM, 65 for AIDP, 159.33±40.21 for PN, 63.66±13.05 for PMLE, 70±22.62 for toxoplasmosis,

184±96.16 for cerebrovascular accident, 165±117.37 for cranial tuberculoma and 92±31.63 in patients with HIV associated dementia [15,16,17].

VI. Conclusion

Present study conclude that the most common neurological illness in HIV patients was tubercular meningitis followed by cryptococcal meningitis, HIV associated dementia, bacterial meningitis, progressive multifocal leucoencephalopathy, peripheral neuropathy and other illness. Neurological illness was most strongly associated with low CD_4 counts. Thus, as a clinician we should focus on neurological involvement and CD_4 count in HIV patients at all stages of illness to reduce morbidity and mortality in patients living with HIV.

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