Original Research Paper

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Neurology

NEUROLOGICAL MANIFESTATIONS OF HIV INFECTION AND IT'S RELATION WITH CD4 COUNT

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KEYWORDS :

BACKGROUND

Acquired Immunodeficiency Syndrome (AIDS) is caused by Human Immunodeficiency Virus(HIV).It is estimated that India had approximately 0.12 million new HIV infections in 2009[1,2]. It is a serious disorder of immune system in which normal defense of body breaks against infection leading to life threatening conditions. The nervous system is among the most frequent and serious target of HIV infection, occurring in patients with profound immune suppression and sometimes neurological disease is the first manifestation of symptomatic HIV infection in10–20% of patients[2,4,5,6]. The true prevalence of HIV related neuro infections and pathology is not available due to inadequate medical facilities, social stigma and ignorance that lead to underdiagnosis[2,7].

In India HIV patient has more chances to manifest full blown AIDS because of poverty and illiteracy. Patient either doesn't take ART or become ART defaulter and due to malnutrition, there are more chances of acquiring co-infection likeTB[3]. The prolonged course of human immunodeficiency virus (HIV) infection is marked by a decrease in the number of circulating CD4+ T helper cells and persistent viral replication, resulting in immunologic decline and death from opportunistic infections and neoplasms[8,9,12].

Acute HIV infection is characterized by a rapid rise in plasma viraemia with a concomitant drop in CD4 count with in 3-6week of exposure[10,12]. Patients with CD4 counts less that 200cells/µl are 19 times more likely to die than those with CD4 counts greater than 350cells/µl.[11,12]

Considering these facts we have decided to study the incidence and clinical profile of various neurological manifestations in HIV patients and their relation with CD4counts.

AIM

To study the clinical profile of various neurological disorders in HIV positive patients.

OBJECTIVES

1 To describe various neurological manifestations in HIV disease
2 To correlate neurological manifestations in HIV patients with CD4 counts.
3 To study the outcome of various neurological conditions in HIV positive patients.

Studydesign: Prospective hospital based observational study.

Study Subjects:

100 HIV positive patients with neurological manifestations admitted in Intensive care unit and medical wards of Sri Venkateswara Ram Narain Ruia Government General Hospital, Sri Venkateswara Medical college ,Tirupati from November 2014toNovember 2015 are the study subjects.

Inclusion Criteria:

1. Patients aged>14years.
2. Patients with neurological manifestations with positive retro viral antibodies.

Exclusion Criteria:

1. Patients with diabetes mellitus, hypertension and cardiac disease.
2. Patients in coma.
3. Patients who have not given consent.

Study Methods :

100patientswhometinclusionandexclusioncriteriainthestudyperiod are included in the study. Detailed history is taken and examination is done in every patient as per the structured proforma. Routine blood investigations, CD4 count, lumbar puncture, chest X-ray and CT scan brain is done in every patient. Other investigations like MRI brain and nerve conduction studies are performed whenever necessary.

RESULTS:

1. Age And Sex Distribution:

Most common age group affected in our study is 21-40 years followed by 41-60 years, both in male and female gender. Least common age group affected in our study is less than 20 years age group(3%). There are no female patients in age group less than 20 years and greater than 60 years. Male preponderance is observed in the present study with a male to female ratio of 2.22:1

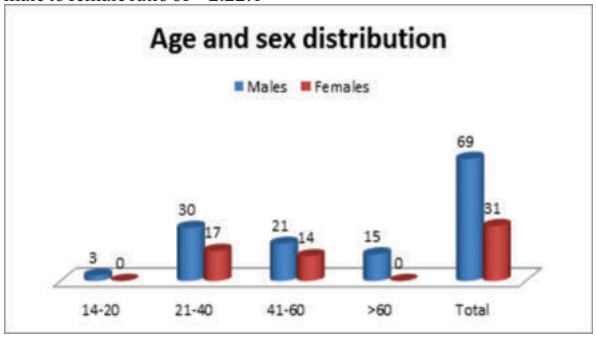

Fig 1: Age And Sex Distribution

2. Presenting Symptoms:

Fever (79%) is the most common presenting symptom in our study followed by headache(75%),vomiting (73%)and altered sensorium (70%).

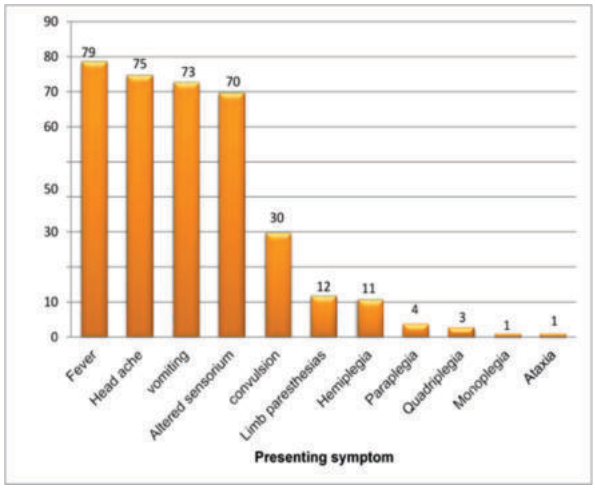

Fig: 2: Clinical Presentation

3. Neurological Diseases :

Mostcommonneurologicaldiseaseobservedinourpatientsismeningitis(71%).Among these, tuberculous meningitis (42%) is most common followed by pyogenic meningitis (15%)and viral meningitis (11%).Other neurological diseases include viral meningoencephalitis(6%),cerebrovascular accident(5%), acute transversemyelitis(4%), acute inflammatory demyelinating polyneuropathy(3%) and distal symmetric polyneuropathy(3%).

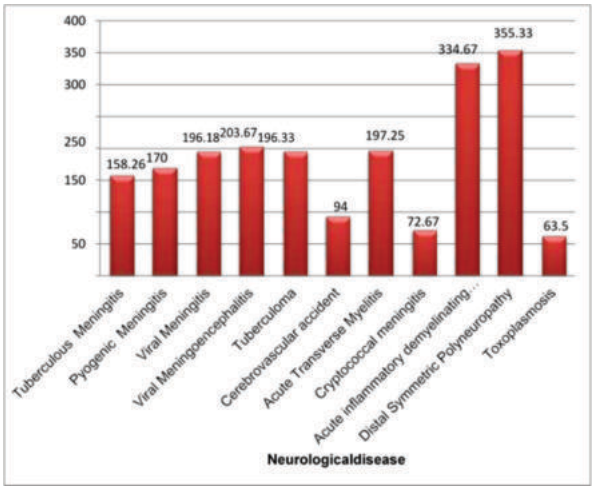

Table :1: Neurological Diseases

S.No.	Neurologicaldisease	Number of Patients	Percentage (%)
1	TuberculousMeningitis	42	42
2	PyogenicMeningitis	15	15
3	ViralMeningitis	11	11
4	ViralMeningoencephalitis	6	6
5	Tuberculoma	6	6
6	Cerebrovascularaccident	5	5
7	AcuteTransverseMyelitis	4	4
8	Cryptococcalmeningitis	3	3
9	Acuteinflammatorydemyelinating polyneuropathy	3	3
10	DistalSymmetricPolyneuropathy	3	3
11	Toxoplasmosis	2	2
	Total	100	100

4. CD4 Counts In Hiv Patients:

Most of the neurological diseases observed in our study had CD4 count between 101-200 percubicmm (38%),followed by CD4 count of less than 100 per cubic mm in 31%.

Table 2: CD4 Counts In Hiv Patients

S.No.	CD4Count per mm3	Number of Patients	Percentage(%)
1	<100	31	31
2	101–200	38	38
3	201- 350	19	19
4	>350	12	12
	Total	100	100

5. Neurological Disease In Relation With Cd4 Count:

21 patients of TB meningitis had CD4 count between 101-200 per cubic mm, followed by CD4 count of less than 100 per cubic mm in 13 patients. Mean CD4 count of TB meningitis is 158.26 ± 91.376 cells percubicmm. Pyogenic meningitis is observed with higher incidence in CD4 count between 201-350 cell per cubic mm followed by less than 200 cells per cubic mm withmeanCD4count of170.00±71.098 cells percubic mm.

Viral meningitis is most commonly observed with CD4 count 101-200percubicmmfollowedby201-350 cells per cubicmm with mean CD4count of 196.18±27.687cellspercubicmm.Cryptococcal meningitis is seen with CD4 of less than 100 cells per cubicmm with mean CD4count of 72.67±14.572cells per cubic mm. Toxoplasmosis is also seen with CD4 counts less than 100 cells per cubic mmwithmeanCD4count of63.50±0.707.

It is also observed in our study that Cerebrovacular accident is seen with CD4count of less than100cells per cubic mm. In contrast to these, Acute inflammatory demyelinating poly neuropathy and Distal symmetric polyneuropathy is observed in patient with CD4 count greater than 350 cells per cubic mm followed by 201-350 cells per cubic mm with mean CD4count of 334.67±90.974 cells per cubic mm and 355.33±58.791 cells per cubic mm respectively.

Table 3: Neurological Disease In Relation With Cd4 Count

S No.	Neurological Disease	CD4count cellspermm3				No of patients	Mean Cd4 count ± SD
		<100	101-200	201-350	>350		
1	Tuberculous Meningitis	13	21	4	4	42	158.26± 91.376
2	Pyogenic Meningitis	4	4	7	0	15	170.00± 71.098
3	Viral Meningitis	0	7	4	0	11	196.18± 27.687
4	ViralMening-oencephalitis	2	2	0	2	6	203.67± 152.034
5	Tuberculoma	2	1	2	1	6	196.33± 108.303
6	Cerebrovas-cularaccident	5	0	0	0	5	94.00± 2.739
7	Acute Transverse Myelitis	0	3	0	1	4	197.25± 133.250
8	Cryptococcalmeningitis	3	0	0	0	3	72.67± 14.572
9	AIDP	0	0	1	2	3	334.67± 90.974
	Distal Symmetric Polyn europathy	0	0	1	2	3	355.33± 58.791
10	Toxoplasmosis	2	0	0	0	2	63.50±0.707

7. Duration Of Hiv Illness:

In our study, majority of patients (40%) were newly detected to be having HIV disease followed by 33% of patients with duration of illness less than one year. 16% had the duration of illness of 1-5 years. Only 11% had duration of illness between 6-10 years.

8. Patients On Haart:

In our study population only 45% were on HAART. Among 55 patients who were not on HAART, 40 patients were newly detected of HIV, 7 patients had duration of HIV illness between 1-5 years, 6 patients had less than 1 year duration and 2 patients had HIV illness between 6-10years.

9. Effect Of Haart On CD4 Count :

In our study 57patients showed the CD4 count between 100-350 cells per cubic mm. Of these 35(61.4%) patients are not on HAART and 22 (38.6%) patients are on HAART. Of the 31 patients who showed the CD4 count of less than 100 cells per cubic mm, 16(51.6%) are not on HAART and 15(48.4%) are on HAART.

12 of the patients showed the CD4 count more than 350 cells per cubic mm and out of these,8(66.66%)of them are on HAART and 4(33.33%) patients are not taking medication.

Table 4. Effect Of Haart On CD4 Count

S No.	Cd4 Count	On HAART(n)	Not onHAART(n)	TOTAL	Percentage (%)
1	>350	8	4	12	12
2	100-350	22	35	57	57
3	<100	15	16	31	31
	Total	45	55	100	100

10. HIV Duration And CD4count:

In our study, 40% of patients were newly detected and 60% were known cases of HIV disease.

Among the 40 newly detected patients, 18 (45%) patients showed the CD4 count between 100-200cells per cubic mm followed by 11(27.5%)patients with CD4 count between 201-350 cells per cubic mm. Only 7 (17.5%)patients showed the CD4 count of less than 100 cells per cubic mm and CD4count of more than 350 cells per cubic mm is observed in 4(10%)of newly detected cases.

Among 32 patients with duration of HIV disease less than one year, 25(78%) patients had CD4 count of less than 200 cells per cubic mm,5

(16%)patients had CD4 count between 201-300 cells per cubic mm and only 2(6%)patients showed CD4 count more than 350cells percubic mm.

16 patients had history of 1-5 years duration of HIV disease. In this group 11 (68.75%) patients showed their CD4 count less than 200 cells per cubic mm, 2 (12.5%) patients had CD4 count between 201-300 cells per cubic mm and CD4 count of greater than 350 cells per cubic mm is observed in only3(18.75%)patients.

The longest duration of disease i.e.,6-10years is observed in 12 patients. Among them 8(66.66%) patients showed their CD4 count of less than 200 cells per cubic mm, 1(8.33%) patient had CD4 counts between 201-300 cells per cubic mm and 3 (25%) patients showed their CD4 count of greater than 350 cells per cubic mm.

Table 5: HIV Duration And CD4count

S. No.	CD4 count	HIV duration				Total
		Newlydetected	<1year	1-5 Years	6-10 Years	
1	>350	4	2	3	3	12
2	201-350	11	5	2	1	19
3	100-200	18	13	4	3	38
4	<100	7	12	7	5	31
	Total	40	32	16	12	100

11. Outcome Of Neurological Manifestations :

In our study majority of the patient (59%) improved without any residual deficit . 13 patients showed residual deficit in the form of either motor weakness or sensory deficit . Among them 5 patients had cerebrovascular accident, 3 had acute transverse myelitis,3 presented with acute inflammatory demyelinating poly neuropathy and one each with distal symmetric poly neuropathy and tuberculoma.

10% of patients were lost to follow up. Mortality is observed in 18% of patients in our study. The common cause of death is TB meningitis seen in 11patients, followed by cryptococcal meningitis in three, pyogenic meningitis in two and toxoplasmosis in two patients.

Table:6 Outcome Of Neurological Manifestations:

S.No.	Outcome	Number of Patients	Percentage (%)
1	Improved	59	59
2	Death	18	18
3	Residual deficit	13	13
4	Lost to followup	10	10
	Total	100	100

DISCUSSION

In the present study the incidence of neurological manifestations is more common (47%) in the age group of 21-40 years followed by 41-60 years with mean age of 43.82 years. The incidence of HIV is more common in age group of 21-40years probably because this is the most sexually active age. The maximum incidence of HIV with neurological manifestations were observed in the age group of 21-40 years in studies done by Sircar et al[13](77.9%), Zeeshan et al[3] (82%) and Sharma et al[2] (90%). Patel et al in their study observed that the mean age was 34.28 ± 7.8 years and in the study by Singh et al it was 40.98 ± 11.42 years

In the present study incidence of HIV infection is more common in males. The male to female ratio is 2.22:1. The higher incidence of male population in our study may be due to their high risk behavior. Similar results were observed in studies by Zeeshan et al[3] (3.2:1) and Singh et al[14] (1.83:1).But male to female ratio was higher in the study of Patel et al[15] (4.5:1) and Sharma et al[2](7:1).

In the present study, most common neurological manifestations are secondary to opportunistic infections than primary to pathological process of HIV infection. The commonest is meningitis. Among the meningitis, TB meningitis is the most common (42%), followed by pyogenic meningitis (15%), viral meningitis(11%), viral meningoencephalitis(6%) and cryptococcal meningitis(3%). Other manifestations include tuberculoma(6%), toxoplasmosis(2%), cerebrovascular accident (5%),peripheral neuropathy(6%) and acute transversemyelitis(4%). According to Mohammed et al[16]. TB meningitis is the most common neurological manifestation in HIV patients (60.3%). The similar results were observed in other studies by Sharma et al[2] (37.5%) and Dhadke et al[17](34%). All the studies correlate with our present study.

Bacterial meningitisis the second most common neurological manifestation in our study which is observed in 15% patients. Study done by Dhadke et al[17] also showed bacterial meningitis as the second most common neurological manifestations seen 14% ofHIV patients which correlates to the present study. But the incidence was less in the studies done by Mohammed et al[16] and Sharma et al[2] where bacterial meningitis was seen in 5.1% and 5.4% of the patients respectively.

The incidence of viral meningitis is 11% in our study. In the study donebyLevyetal[18]viral meningitis was seen in 11.01% patients which correlates to our study. Lower incidence of viral meningitis was observed in the studies done by Deshpande et al[19] and Wadia et al[20] which was 1.33% and1.11% respectively.These results do not correlate with our study. In our study, Cryptococcal meningitis is seen in 3% of patients. Similar results were observed in the studies done by Dhadkeet al[17] (4%) and Singhet al[21] (6.01%). In the studies done by Mohammed et al[16] and Sharma etal[2]cryptococcal meningitis was seen in higher percentage of patients.

The incidence of viral meningoencephalitis is 6% in our study. But the results of the study by levy et al[18] showed a very high incidence of viral meningoencephalitis(34%). In the studies done by Mohammedetal[16],Sharma et al[2] and Singh et al[21] there was not even one patient with viral meningoencephalitis.

The commonest intra cranial space occupying lesion (ICSOL) in our is tuberculoma (6%). Similar results were observed in the study of Sharma et al[2](5%) and Mohammed et al[16] (3.4%). The incidence of tuberculoma is higher(14%) in the study by Dhadkeetal[17]

Toxoplamosis is the second most common ICSOL in our study (2%).Similar results were observed in studies done by Dhadke et al[17] (2%) and Singhetal[21](1.2%).

In the present study cerebrovascular accident is seen in 5% of patients. Similar results were observed in studies of Mohammed et al[16] (8.6%) and Sharma et al[2] (7.5%). Butan increased incidence of cerebro vascular accident was observed by Dhadke etal[17](14%).Peripheral neuropathy is seen in 6% of patients in the present study. Similar observations were made by Levy et al[18] (6%), Dhadke et al[17] (8%) and Singh et al[21](10.1%). There was lower incidence of peripheral neuropathy in the study by Mohammed et al[16] (1.7%) and increased incidence was seen in the study by Sharmaetal[2](20%). These do not correlated with our study. Mc Arthur et al[22] showed that the incidence may increase by the toxic effects of specific antiretroviral drugs on the peripheral nervous system. In our study the peripheral neuropathy is probably due to primary illness itself as most of our patients were drug naïve and the chance of drug induced neuropathy is less.

In our study CD4 count is <200 cells per cubic mm in 69% of patients. In the study done by Patel et al[15] 48.89% had CD4 counts less than 200 cells per cubic mm. Singh et al[21] observed CD4 count less than 200 cells per cubic mm in 88.23% of study subjects. Similar observations were made by Sharma et al[2] (64%) and Dhadke et al[17] (76%). All these results correlate with our present study suggesting that neurological manifestations occur more frequently with low Cd4counts..

In the present study most of the patients (69%) have CD4 count oflessthan200cells/mm^3 followed by 201-350cells/mm^3 (19%)and>350cells/mm^3 (12%).In the study done by Patel etal[15]most of the patients (48.89%) had CD4 count of less than 200 cells/mm^3 followed by 201-350cells/mm^3 (33.33%), and >350 cells/mm^3(28.57%). This results correlate with our present study.

In the present study mean CD4 count in TB meningitisis 158.26±91.376 cells per cubic mm which correlates with the studies done by Sharma et al[2] and by Singh et al[21] where mean CD4 count was less than 200cells per cubic mm in TB meningitis.

The mean CD4 count in patients with viral meningitis is 196.18±27.687cells per cubic mm in the present study. In the study done by Singh et al[21] the mean CD4 count in viral meningitis (CMV) is 107±113 cells per cubic mm showing a wide range.

In the present study mean CD4 count of cryptococcal meningitis is 72.67±14.572 cells per cubic mm. Similar results were observed in studies by Singh et al[21] and Patel et al[15] in which CD4 count is less than 100 cells per cubic mm.

Our study showed mean CD4 count of 196.33±108.303 cells per cubic

mm in tuberculoma. In the study by Singhetal[21] the mean CD4 count in space occupying lesions like tuberculoma and brain abscess is less than 200 cells per cubic mm. This result is more or less similar to our present study.

In the present study mean CD4 count of toxoplasmosis is 63.50±0.707cells per cubic mm. Study by Singh et al[21] correlates with our study with meanCD4 count in toxoplamosis less than 100 cells per cubic mm. In the studies done by Patel et al[15] and Zeeshan et al[3] mean CD4 count in toxoplasmosis is greater than 100 cells per cubic mm showing that it can even occur at moderate degree of immune supression

Mean CD4 count of 94.00±2.739 cells per cubic mm is observed in cerebrovascular accident in our study. Similar observations were made by Singhetal[21] in their study. In the present study patients with acute inflammatory demyelinating polyneuropathy have higher mean CD4 count of 334.67±90.974 cells per cubic mm which is comparable to study done by Patel et al[15] indicating that acute inflammatory demyelinating polyneuropathy is more common in patients even with mild degree of immunosupression. In the study done by Singhetal[21] mean CD4 count was 110 cells per cubic mm in patients with acute inflammatory demyelinating polyneuropathy which is far less compared to our present study.

Mean CD4 count observed in our patients with distal symmetric polyneuropathy is greater than 350 cells per cubic mm i.e., 355.33±58.791cells per cubic mm. In the studies done by Patel et al[15] and Singh et al[21] meanCD4 count in patients with distal symmetric polyneuropathy was less than 200cells per cubic mm. These results are not similar to our present study. In the present study mean CD4 counts are less than 200 cells per cubic mm in patients with viral meningitis and acute transverse myelitis indicating that these manifestations occur in severe degree of immunosupression.

In our study, majority of patients (40%) were newly detected to behaving HIV disease. In the study done by Mohammed et al[16] 62% were newly diagnosed cases of HIV disease. This correlates with our study. Poverty, illiteracy and lack of health education may be the reasons for late detection of HIV only when the patient presents with neurological manifestation.

In the present study, 40 patients were newly detected cases and 60 patients were known cases of HIV infection. Among 60 patients, 48 patients were on HAART. Remaining 12 patients were not taking medication.

In the present study, 57 patients showed their CD4 count between 100-350 cells per cubic mm. Among them 35 patients were not on HAART and only 22 patients are on HAART. 31 patients showed their CD4 count of less than 100 cells per cubic mm. Among them 15 are not on HAART and 16 are on HAART.12 patients showed their CD4 count more than 350 cells per cubic mm. Among them 10 patients are on HAART and only 2 patients are not on HAART. Our study shows no statistically significant correlation between CD4count and usage of HAART medication. In the study done by Caggiari et al[23] It was shown that CD4 count increases by HAART and it does not correlates to our present study.

In our study, 40% of the patients were newly detected and 60% were known cases of HIV disease. There was no statistically significant correlation between duration of HIV and CD4 count in our study. This is probably because those patients who were newly detected as HIV positive at the time of presentation will have a wide variation in duration from the time of initial exposure to the detection of HIV status and also CD4 count varies with the duration and compliance of HAART.

In the present study majority of the patient (59%) improved without any residual deficit. In the study done by Patel et al[15] it is observed that majority of the patients (81%) improved which correlates with our study.

The mortality rate of present study correlates with the study done by Patel et al[15] which shows a mortality rate of 19%. Zeeshan et al[3] observed higher mortality rates (46%) and correlation with CD4 count. Our study showed no statistically significant correlation between mortality rate and Cd4count.

CONCLUSION

HIV with neurological manifestations is commonly observed in sexually active age group, Commonest presenting symptoms are fever, headache, vomiting and altered sensorium. Commonest neurological manifestation observed is tuberculous meningitis. Neurological manifestations observed irrespective of duration of HIV disease, CD4 count and treatment (HAART).

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