

Original Research Article

A study on clinical profile of neurological manifestations among HIV infected patients attending a tertiary care hospital of south India

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ABSTRACT

Background: Current statistics show that 36.9 million (31.1-43.9 million) people were living with HIV globally at the end of 2017. 15-73% of people with HIV may develop neurological disorders with sometimes as a presenting illness. The aim of present study is to document the various neurological manifestations and presentations with relation to CD4 counts among the HIV/AIDS cases attending a tertiary care hospital of south India.

Methods: A prospective study was conducted for two years at a tertiary care hospital among confirmed cases of HIV and the neurological manifestations were diagnosed and clinical signs and symptoms were noted. CD4 counts of all the cases were performed by FACS counter and Neuroimaging study was performed on necessary cases.

Results: Total of 125 cases with 69.6% males and 30.4% females were enrolled. Mean age of cases was 35.14±3.8years. 86.4% were positive for HIV-1 type. Headache was the most common ailment (78.4%). Meningeal enhancement observed in 24.5% followed in order by ring enhancing lesion (18.37%), cerebral atrophy and infarction (12.24%). Tubercular meningitis was the commonest type (33.6%). In 12 cases of cryptococcal meningitis the CD4 counts were <100 cells/mm³.

Conclusions: To conclude in present study, secondary neurological manifestations were more common than primary manifestations in present study. Tubercular meningitis being the most common and CD4 counts <100cells/mm³ were associated with cryptococcal meningitis. Cases with CD4 counts less than 100cells/mm³ had poor prognosis.

Keywords: AIDS, CD4 count, Cryptococcal meningitis, HIV, Tubercular meningitis

INTRODUCTION

Globally the incidence of HIV is still on a surge of increase in spite of various control measures adopted by the international health organizations. Current statistics show that 36.9 million (31.1-43.9 million) people were living with HIV globally at the end of 2017. This burden of epidemic varies from region to region and place to place. The sub Saharan and African regions are the severely affected region with followed by the south East Asian countries. The regional prevalence of HIV infection is about 25 times higher in African region than south east Asian region. In India the incidence of HIV is

on a drop with total number of people living with HIV is estimated at 21.40 lakhs in 2017 as per the India HIV estimation data report 2017.¹ The current CDC classification HIV is based on the clinical conditions associated with the CD4 counts. The clinical conditions which arise from immune deficiency due to lowering of CD4 and CD8 cell counts are highly variable and depend on which organ or system of the body is involved. Minor diseases like herpes zoster, candidiasis may precede the development of severe AIDS. The respiratory, gastro intestinal and central nervous system are common sites of complications in HIV/AIDS.²

Around 15-73% of people with HIV may develop neurological disorders with sometimes as a presenting illness. Neurological disease is a presenting manifestation in 10-20% of HIV affected individuals. Every component of the nervous system including central and peripheral are affected leading to a wide array of disorders which may range from simple peripheral neuropathy to demyelinating disorders. The polyclonal hypergammaglobulinemia induced by the virus affects the CNS early and results in demyelinating disease of CNS and peripheral nervous system.³ Most of the autopsy studies in HIV deaths have revealed neuro pathological manifestations indicating that most of the neurological disorders are unidentified and may be a cause of death. Hence the knowledge of neurological disorders affecting the CNS in cases of HIV/AIDS is most important to the clinician. With the advent of highly active antiretroviral therapy (HAART) the life span of patients with HIV has increased and neurological disorders has become protean.⁴ Therefore there is a grave need to study the changing pattern of neurological disorders among cases of HIV. The present study documents the various neurological manifestations and presentations among the HIV/AIDS cases attending a tertiary care hospital of south India.

METHODS

A prospective observational study was conducted at a tertiary care hospital of south India for a period of two years from January 2016 to December 2017. The study was approved by the institutional ethical committee and conducted as per the guidelines of the committee. Details of the study were explained to all the cases and written consent was obtained from all the cases who consented to participate in the study. Patients with a confirmed status of HIV attending the OPD of department of general medicine with a sign of neurological manifestations were enrolled in the study after fulfilling the inclusion criteria. HIV status of the cases in the study was confirmed as per the guidelines of National AIDS control programme by detection of antibody on two successive samples using a third generation ELISA kit and if found positive a third sample is collected and tested using HIV-1/HIV-2 assay using Bio-Rad diagnostic test kit. Cases attending the ART center were also included in the study after fulfilling the inclusion criteria. A thorough clinical history, clinical examination with socio demographic data, drug history, co-morbidities e.g., diabetes, alcohol abuse, drug abuse, epilepsy were noted. Routine haematological, biochemical investigations and CD4 counts were done in all the cases enrolled in the study. Imaging modalities that were performed included MRI, CT of brain and chest X-ray among the cases whenever required as per the study protocol. CSF investigations included biochemical, microbiological and cell counts were performed in all the cases of meningitis. Indian ink preparation of CSF was done in suspected cases of cryptococcal meningitis. Anti-toxoplasma antibody detection by using ELISA (Bio-Rad ELISA kit) was done

and confirmed in suspected cases of toxoplasmosis. CD4 counts were performed by using flow cytometer using syflow counter. (FACS counter) All the data collected was entered in Microsoft excel and analyzed.

Inclusion criteria

All the patients above 18 years of age who consented for the study were included in the study.

Exclusion criteria

- Patients with known history of CNS disturbances
- Epilepsy
- Alcohol abuse
- Drugs causing neurological disturbances

Statistical analysis

The collected data was entered in Microsoft excel spread sheet and analyzed. The data was expressed as means and medians with percentages and proportions. P value of <0.05 was considered significant.

RESULTS

The present study was conducted for a period of two years at a referral tertiary care hospital of south India catering an overall population of 5 lakhs. A total of 125 confirmed cases of HIV who fulfilled the inclusion criteria and consented for the study were enrolled. Males were predominant with 69.6% (87/125) and females 30.4% (38/125). Male to female ratio in the study was 2.3:1. The mean age of the study group was 35.14±3.8 years with male's 31.28±5.4 years and females 30.58±4.5 years. Majority of the cases were in the age group of 18-30 years (38.4%) followed in order by 31-40 years (35.2%), 41-50 years (16.8%) and >50 years (9.6%) (Table 1).

Table 1: Demographic data of cases in the study.

Demographic character	No.	%
Males	87	69.6
Females	38	30.4
Total	125	
M:F ratio	2.3:1	
Mean age of cases (years)	35.14	
Mean age of males (years)	31.28	
Mean age of females (years)	30.58	
Age group (years)		
18-30	48	38.4
31-40	44	35.2
41-50	21	16.8
>50 years	12	9.6

Most common mode of transmission among male cases in the study was contact with commercial sex workers (CSW) (96.6%), and among females 28 cases (73.7%)

acquired infection from HIV positive husbands, 6 were CSW and 4 acquired from contaminated blood transfusion. In 3 cases the source of transmission was unknown. 108 cases (86.4%) were positive HIV-1 serotype, 13 (10.4%) for HIV-II and 4 (3.2%) for both HIV-type-I and II. 114 cases were married (91.2%) and 11 cases (8.8%) were single.

Table 2: Distribution of symptoms of neurological manifestations among cases in the study.

Symptoms	No.	%
Fever	89	71.2
Headache	98	78.4
Vomiting	78	62.4
Altered sensorium	64	51.2
Convulsions	72	57.6
Vertigo	12	9.6
Focal neurological deficit	24	19.2
Cranial abnormality	10	8
Sensory abnormality	14	11.2
Behaviour abnormality	8	6.4
Blurring of vision	6	4.8

Table 2 summarizes the distribution of various signs and symptoms among the cases in the study. Headache was the most common ailment (78.4%) followed by fever (71.2%) and vomiting (62.4%). Convulsions were observed in 57.6% of cases followed by altered sensorium (51.2%), focal neurological deficit in 19.2%, sensory abnormality in 11.2% and other less common features include vertigo (9.6%), cranial abnormality (8%) and Behaviour abnormality (6.4%). Neuro imaging of brain was done among 98 cases in the study and the findings are summarized in Table 3. 12.24% of cases revealed normal study while the major finding was meningeal enhancement observed in 24.5% followed in order by ring enhancing lesion (18.37%), cerebral atrophy and infarction (12.24%). Less common were hydrocephalous (8.16%) and encephalitis and tuberculoma with infarct (6.12%).

Table 3: Neuro imaging findings among the cases in the study.

Finding	No (n=98)	%
Normal	12	12.24
Meningeal enhancement	24	24.49
Infarction	12	12.24
Ring enhancing lesion	18	18.37
Cerebral atrophy	12	12.24
Hydrocephalous	8	8.16
Encephalitis	6	6.12
Tuberculoma and infarct	6	6.12

Table 4 summarizes the various neurological manifestations in cases of the study. Meningitis was the commonest with 62 cases, tubercular being the commonest 93.6%), cryptococcal (9.6%) and bacterial

(6.4%). 12 cases (9.6%) had AIDS dementia complex and 12 cases (9.6%) with herpes zoster involvement. Less common manifestations in the study group was toxoplasmosis in 2 cases, infarct in 8 cases, Demyelinating polyneuropathy in 5 cases and progressive multifocal leukoencephalopathy in 4 cases of the study. Painful paraesthesias and peripheral neuropathy were common features in AIDS cases in the study.

Table 4: Neurological diagnosis of cases in the study.

Manifestations	No.	%
Meningitis		
Tubercular	42	33.6
Cryptococcal	12	9.6
Bacterial	8	6.4
AIDS dementia complex	12	9.6
Infarct	8	6.4
Demyelinating polyneuropathy	5	4
Progressive multifocal leukoencephalopathy	4	3.2
Toxoplasmosis	2	1.6
Herpes simplex / zoster	12	9.6

Table 5 summarizes the CD4 counts of cases in the study. 33.6% of cases had counts between 200-500, 53.65% with counts 100-199 and 12.8% with counts <100cells/mm³. The mean CD4 count of the cases in the study group was 218.0±85.3cells/mm³. Among the 12 cases of cryptococcal meningitis the CD4 counts were <100cells/mm³.

Table 5: Distribution of CD4 cells among the cases in the study.

CD4 count (Cells/mm ³)	No.	%
200-500	42	33.6
100-199	67	53.6
<100	16	12.8

DISCUSSION

The prevalence of neurological manifestations both primary and secondary is protean in nature and differs from region to region and place to place. Evidences gathered from studies universally portray that neurological complication among HIV individuals increase with severity of immune suppression and pose a constant awareness and challenge to the physicians in management and diagnosis.⁵ In the present study, the incidence of neurological manifestations among HIV infected individuals was 14.6% which when compared with the findings of Wadia et al, was very low who reported an incidence of 24.8% in his report but was on par with the findings of Millogo et al, who reported 15% incidence in his study.^{6,7} these variations in the incidence are mainly due to differences in the cultural practices and differences in the ethnic population and genetic factors. In the present study, the most common age group was

between 18-30years which is the highly economically productive group. Various studies also reported similar age group as the most commonly affected age group in their studies. Males were predominantly affected gender as described in various studies globally because they are working and more exposed to commercial sex workers when they go far from family to earn and with increased risk of blood transfusion and drug abuse. Male to female ratio in present study was 2.3:1 whereas John et al, reported 4.26:1 in his study which differs from the present study.⁸ The most common mode of transmission was heterosexual route by contact with CSW in present study which is similar to the reports of NACO and studies of Bollinger et al.⁹ This disparity between the studies reported in the western literature and Indian studies can be explained by the different cultures and pattern of sexual activity in respective society. In present study, HIV type -I was the most common serotype and similar to many studies conducted in various parts of south India.

The neurological manifestations that occur in cases of HIV may be due to primary pathological process of HIV or secondary to infections or neoplasm. In our study, Headache was the most common ailment (78.4%) followed by fever (71.2%) and vomiting (62.4%) similar findings close to our study was found in reports of Pal et al but contrary to the findings of Berjer et al, who reported headache as the most common ailment in his study.^{10,11} Seizures were observed in 57.6% of cases in the study and may be a consequence of HIV encephalopathy, neoplasms or opportunistic infections. A few of the studies from western countries reported intra cranial space occupying lesion (ICSOL) as most common cause of seizures in HIV individuals. Altered sensorium was observed in 51.2% of cases in present study which is similar to the findings of Sircar et al who reported 54% in his study but contrary to the findings of Skolasky RL et al, who reported as low as 22% in his study.^{12,13} Focal neurological deficit was observed in 19.2% of cases in present study which was similar to the findings of Antinori A et al, who reported 24% of cases of FND in their study.¹⁴

Meningitis was the most common neurological manifestation in the cases of present study with tubercular being the commonest. These findings were almost on par with the findings of Kwan CK et al, who reported TBM as the most common cause of meningitis in India whereas findings from western studies state that cryptococcal meningitis as the common secondary opportunistic infection.¹⁵ Meningeal enhancement was observed in 24.5% of cases and was the most common Neuroimaging finding observed in the study and similar findings were reported in the study of Cohen et al, and Rana HM et al.^{16,17} Maschke M et al, in their study reported AIDS dementia complex (ADC) as the most common manifestation which is contrary to the findings of present study. This is due to the differences in the prevalence of different serotype and genetic factors prevalent in the study population.¹⁸ Demyelinating

polyneuropathy and progressive multifocal leukoencephalopathy were less common in present study, but few studies abroad have reported an increasing trend in the disorders after the advent of HAART therapy. Studies have also reported the presence of neurological complication as well as other clinical manifestations associated with decreased CD4 count and increased viral load which is consistent with our study and Secondary manifestations were more common in cases with CD4 counts <100cells/mm³. The mean CD4 count of the cases in the study group was 218.0±85.3cells/mm³ which is found to be almost similar to the Mansuri ZH et al, who reported the mean count as 228.0±38.14cells/mm³.¹⁹ However cases with CD4 counts <100cells/mm³ had poor prognosis. Tubercular meningitis was the most common manifestation in our study irrespective of CD4 counts.

CONCLUSION

To conclude in present study, secondary neurological manifestations were more common than primary manifestations in present study. Tubercular meningitis being the most common and CD4 counts <100cells/mm³ were associated with cryptococcal meningitis. Cases with CD4 counts less than 100 had poor prognosis. These developing changes in the cases of HIV may be due to longer life span in the cases which is due to active HAART therapy. Moreover HIV itself presented with various neurological problems throughout the infection. These patterns of infections are different from the developed countries due to differences in the serotype causing the infection, socio economic transmission and genetic factors.

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