

Magnetic Resonance Imaging Evaluation of CNS Diseases in AIDS Patients and Correlation of CD4+ Cell Count with the Opportunistic Infections

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DOI: <http://dx.doi.org/10.21276/ijcmsr.2021.6.2.2>

How to cite this article: Jaybrata Ray, Prabhat Debbarma, Tanusri Debbarma. Magnetic resonance imaging evaluation of CNS diseases in AIDS patients and correlation of CD4+ cell count with the opportunistic infections. International Journal of Contemporary Medicine Surgery and Radiology. 2021;6(2):B6-B11.

ABSTRACT

Introduction: The CNS is involved in 39-70% of cases of HIV infection. Pathologically >90% of the patients with AIDS show brain lesions. Morbidity due to CNS lesions is estimated to be around 30%. Early diagnosis of various CNS lesions provides an opportunity to treat the diseases at an early stage and decrease the mortality and morbidity and prolong the survival of the individual. **Aims:** The study was carried out to study the prevalence of different types of central nervous system lesions and to find out the relationship between opportunistic infections and CD4 + count in AIDS patients. **Settings and design:** Hospital based Cross sectional study conducted in a single academic institute with a high number of HIV/AIDS patients.

Material and methods: Fifty (50) patients were examined between age group 18 – 60 years for a period of two years from June 2009 to December 2011.

Results: Most of the cases were seen among the males in the age group of 20 – 40 years. The commonest neurological disease seen was CNS tuberculosis followed by HIV encephalitis, cerebral infarction and PML. CMV encephalitis, Toxoplasmosis and cryptococcosis were seen in fewer numbers of cases. Most of the cases of opportunistic infections (n = 29) had a CD4 count below 100.

Conclusions: Changing epidemiological trend is seen as the prevalence of disease is increasing in females and sexual transmission becoming more common. Disease is seen more commonly in higher age group. Tuberculosis has emerged as the commonest disease replacing toxoplasmosis. Higher CD₄ count is seen in all patients.

Keywords: HIV/AIDS, Brain, MRI, Opportunistic Infection, Tuberculosis, Infarction, HIV Encephalitis, Toxoplasmosis, CD4 Count.

Key Messages: MRI of brain is essential in AIDS patients for a proper diagnosis and assessment of response to treatment. Spectrums of opportunistic infections are changing with the advent of HAART and also the relationship between CD₄ counts.

INTRODUCTION

The Human Immune deficiency virus (HIV) infects the brain commonly and at a very early stage of the disease. The Central nervous system (CNS) is involved in 39-70% of cases of HIV infection and pathologically >90% of the patients with AIDS show brain lesions.¹ The primary CNS lesions include brain atrophy, white matter lesions, HIV demyelination, progressive multifocal leucoencephalopathy (PML) and encephalitis. The secondary HIV related lesions include space occupying lesions such as tuberculoma, cryptococcosis, candidiasis, lymphoma, toxoplasmosis etc. Morbidity due to CNS lesions is estimated to be around 30%. Out of this the commonest CNS lesion in HIV positive patients is subacute encephalitis and commonest secondary

opportunistic infection is toxoplasmosis.²

Early diagnosis of various CNS lesions provide an opportunity to treat the diseases at an early stage decreasing the mortality, morbidity and prolong the survival of the individual. Serological tests are often unhelpful in diagnosis of CNS opportunistic infections due to poor immunological response of AIDS patients and also due to high prevalence of infection in community. Neuroimaging is of immense value in such cases and MRI of brain is the investigation of choice for evaluation of different neurological diseases.³

The clinical spectrum of disease caused by opportunistic infections (OIs) constantly changes from time to time. Also CD₄ lymphocyte count and the distribution of diseases most commonly found in AIDS patients differ from one area to other. When CD₄ count falls below the critical level of <200

cells/ μL , patients become susceptible to OI². The more severe and life threatening complications of AIDS occur in patients with CD₄ count < 200 cells/ μL .⁴

Coinfection with HIV, Hepatitis C virus (HCV) and Hepatitis B virus (HBV) is a growing public health concern and after the introduction of highly active antiretroviral therapy (HAART), liver disease has emerged as a major cause of morbidity and mortality in HIV-infected persons.⁵ This study was intended to determine the prevalence of different brain lesions in AIDS patients so that necessary steps may be taken to treat these patients early, increasing therapeutic response to HAART and thus reducing mortality and morbidity.

Aims and objectives

1. To study the prevalence of different types of central nervous system lesions by MRI of brain in AIDS patients.
2. To find out the relationship of opportunistic infections and CD4+ count in AIDS patients.

MATERIAL AND METHODS

The study was carried out in the Department of Radiodiagnosis, RIMS, Imphal for a period of 2 years w.e.f. August 2009 to July 2011. The patients were selected by systematic random sampling with sampling interval zero. As this is a hospital based study & MRI is an expensive diagnostic modality the sample size was taken fifty (50). Fifty (50) patients of clinically diagnosed AIDS patients between 18 – 60 years were studied by MRI. The patients who had past history of neurological disease and were on CNS medications were excluded from the study. Standard diagnostic definitions were used during image analysis. MRI examination of brain was done in “SIEMENS 1T MAGNETOM 2004A”. Standard T1, T2 SE axial, sagittal, coronal, axial FLAIR, axial diffusion weighted sequences were obtained routinely. Gadolinium enhanced axial, coronal and sagittal sequences were whenever deemed necessary. This study was approved by the institutional ethical committee. Informed consent was obtained from all the cases before including them in the study. Detailed history was obtained. Routine investigations as complete hemogram, RBS, LFT, KFT was done. CD4 count, HBsAg and anti HCV serology status were performed for all patients. CSF IgG and IgM antibody titer for toxoplasmosis, cryptococcosis, cytomegalovirus and India Ink preparation of CSF were done in all cases. Standard diagnostic criteria were used all throughout the study for image analysis and clinical correlations with treatment response were also taken into account. Special statistical software ‘SPSS version 15’ was used for data analysis.

The MRI protocols used were

T1W IMAGES (TR 500ms, TE 14ms).

T2W IMAGES (TR 4000ms, TE 99ms).

FLAIR (TI 2500ms, TR 9000ms, TE 112ms).

DIFFUSION STUDY (b0, b600, b900).

RESULT

Out of 50 patients 33 (66%) were male and 17(34%) were female with male to female ratio of 1.94 : 1. Hindus

contributed to 24 (48%) and Christians contributed to 26 (52%) patients. 24 (48%) cases were intravenous drug users and 25 (50%) were sexually transmitted disease. Only one patient had transmitted the disease by blood transfusion. 20 (40%) patients were in the age group of 30 – 39 years, 19

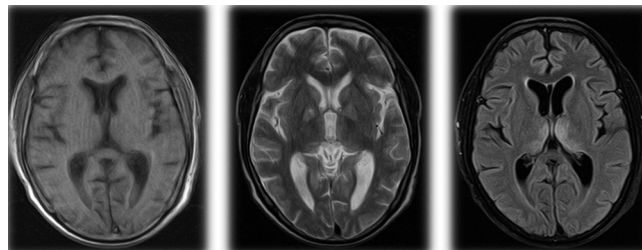


Figure-1: T1, T2 and flair mri images showing features of hiv encephalitis – mild atrophy of frontal region with focal hyperintense lesions in T2 and flair images in bilateral basal ganglia and thalamus.

CNS disease	No of cases
CNS tuberculosis	10
HIV encephalitis	9
Infarction	8
PML	7
CMV encephalitis	4
Toxoplasmosis	4
Cryptococcosis	4
Demyelination	1

Table-1: Profile of neurological diseases in aids patients

Disease	Mean CD ₄ count (cells/ μL)
Cryptococcosis	37.5
Toxoplasmosis	56.25
PML	88.5
HIV demyelination	89
CMV encephalitis	104
CNS tuberculosis	122
HIV encephalitis	183.5
Cerebral infarction	238.5

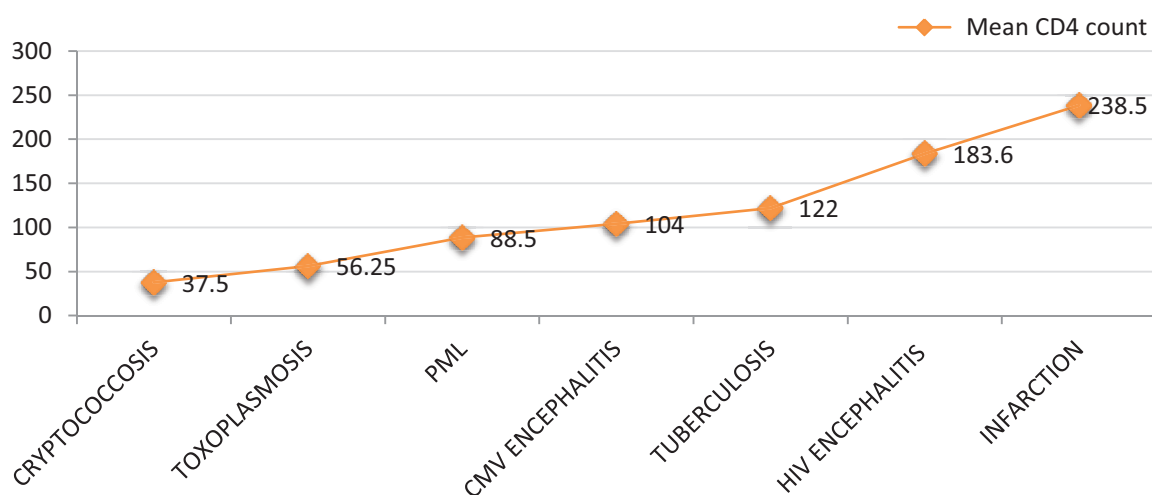
Table-2: Relation between mean CD4 count and neurological diseases

CD ₄ count	No of cases
0-50	10
51- 100	12
101 - 150	14
151 - 200	7
>200	7

Table-3: CD4+ cell count in aids patients

CD4+ count	OI present	OI absent	Total
0-200	29	14	43
201-500	0	7	7
Total	29	21	50

Table-4: Distribution of opportunistic infections according to CD4+ cell count



Graph-1: Showing correlation between mean CD4 count & CNS diseases

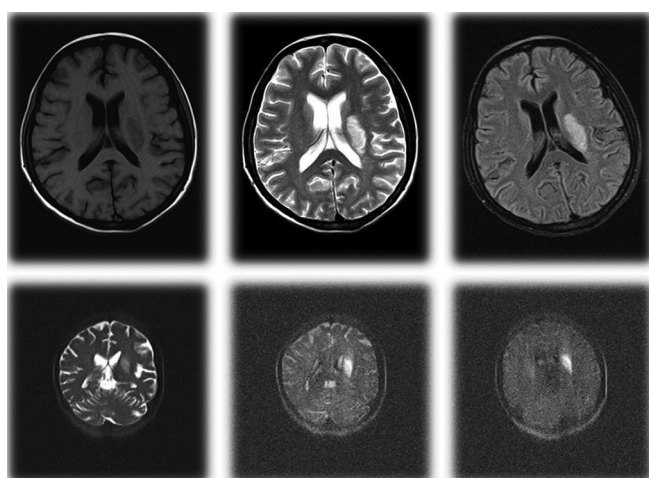


Figure-2: T1, T2, flair and dw images showing features of infarction – oval lesion in left basal ganglia which is hypointense in T1, hyperintense in T2, flair, dw images.

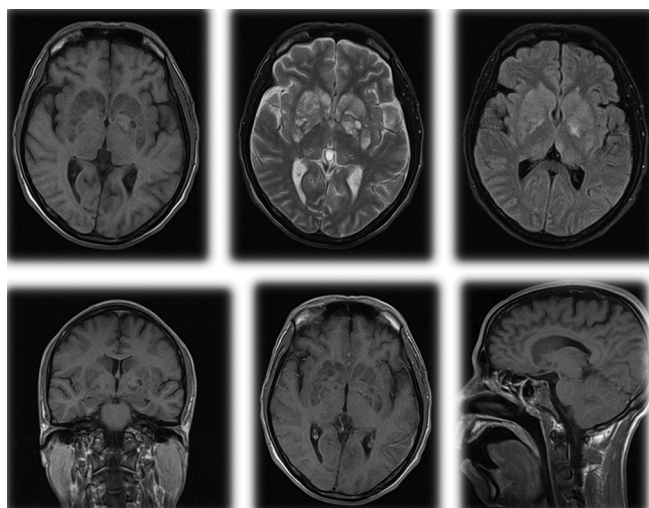


Figure-3: T1, T2, flair and contrast enhanced t1w images in a case of CNS cryptococcosis – multiple small hypointense lesions in bilateral basal ganglia which are hyperintense in T2, flair and dw images.

(38%) were from 40 – 49 years age group, 8 (16%) were from the age group of 20—29 years and 3 (6%) were from the age

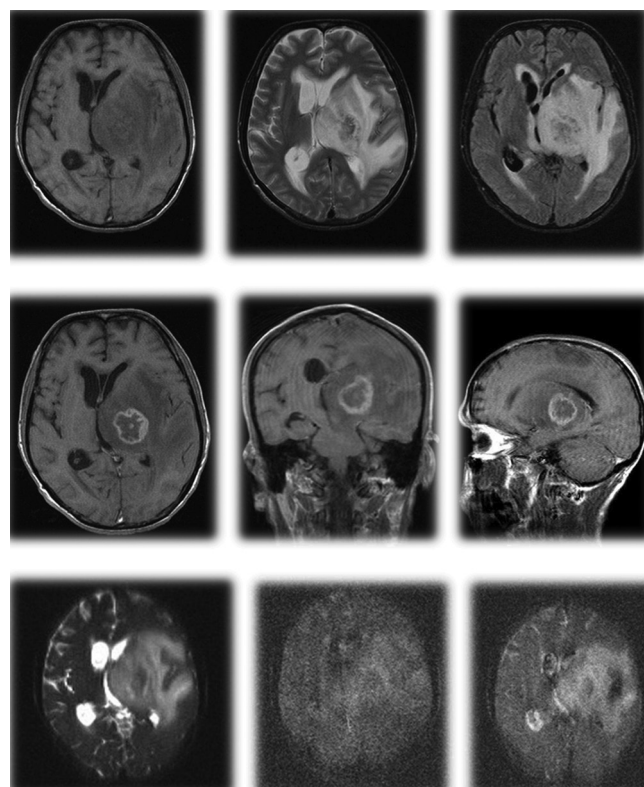


Figure-4: T1, T2, flair, DW images with contrast enhanced images in a case of cerebral toxoplasmosis – a large ring enhancing lesion in left basal ganglia with mass effect, midline shift, central necrosis.

group of >50 years. 46 (92%) of the cases were married and only four (8%) were unmarried. Out of 50 cases four (8%) were HBsAg positive nine (18%) were anti HCV positive and one patient was positive for both HBsAg and anti HCV. The commonest neurological disease seen was CNS tuberculosis which accounted for ten (20%) cases with a mean CD₄ count of 122 cells /μL. HIV encephalitis accounted for nine (18%) cases with mean CD₄ count of 183.3 cells/μL. Cerebral infarction was seen in eight (16%) cases with mean CD₄ count 238.5 cells /μL. PML was seen in seven (14%) cases with a mean CD₄ count of 88.5 cells /μL. CMV encephalitis, Toxoplasmosis and cryptococcosis accounted for four (8%) cases each. Mean CD₄ count was 104 cells/μL, 56.25 cells/μL and 37.5 cells/μL respectively.

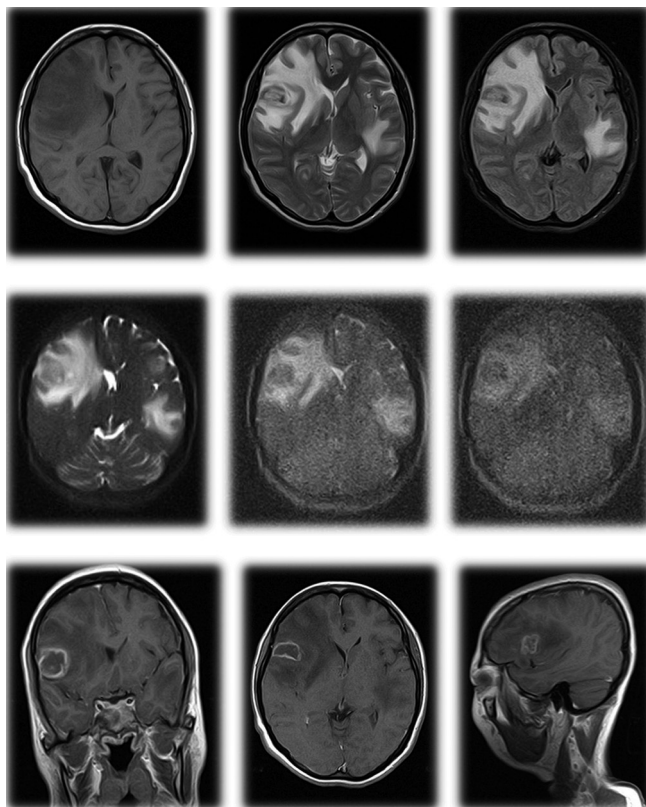


Figure-5: T1, T2, flair, DWI And contrast enhanced images in a case of CNS tuberculoma – multiple rim enhancing lesion in the corticomedullary junction of right frontal lobe and left parietal lobe with mass effect, midline shift and central necrosis.

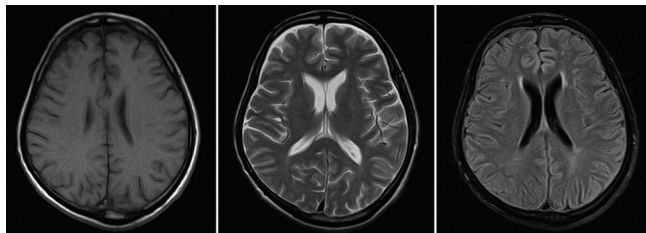


Figure-6: T1, T2 and flair images showing HIV demyelination – multiple small punctate T2 hyperintensities in both frontal lobes and basal ganglia.

HIV demyelination was seen in one case only. In this study Cryptococcal meningitis was the disease which was seen with mean CD₄ count <50 cells/μL. Progressive multifocal leukoencephalopathy and toxoplasmosis were seen when mean CD₄ count was between 50 – 100 cells/μL. CMV encephalitis and CNS tuberculosis were seen when mean CD₄ count was between 100 – 150 cells/μL. HIV encephalitis was seen when mean CD₄ count was between 151 – 200 cells/μL and cerebral infarction was seen when mean CD₄ count was >200 cells/μL. Mean CD₄ count was lowest in cases of cryptococcosis and highest in cases of cerebral infarction. In this study 14 (28%) patients had a CD₄ count between 101 – 150 cells/μL. Next most common group had CD₄ count of 51 – 100 cells/μL, the number of patients being 12(24%). 10(20%) patients had CD₄ count between 0 – 49 cells/μL and. Seven (14%) patients had CD₄ count >200 cells/μL. Altogether 86% of the cases had CD₄ count <200 cells/μL. Mean CD₄ count in this study was 115 cells/μL.

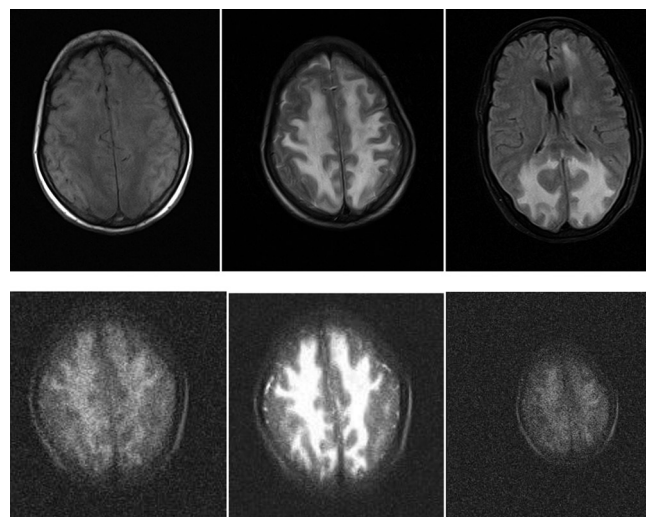


Figure-7: T1, T2, flair and DWI showing PML in a case of AIDS – diffuse confluent hypointense lesions involving both parietal and occipital lobes which are hypointense in T1 and hyperintense in T2, flair and DWI images.

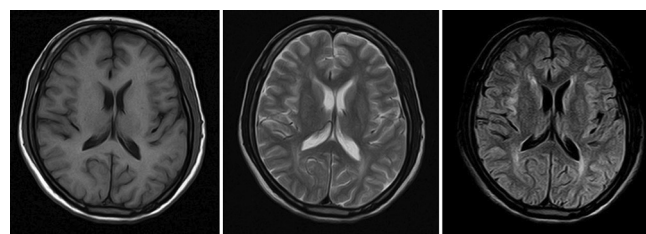


Figure-8: T1, T2 and flair images showing CMV encephalitis in a case of AIDS with ocular CMV infection – multifocal small T2 hyperintense lesions in the periventricular white matter region, gray-white junction and along the cortical gyri in the bilateral parietofrontal region.

DISCUSSION

Slightly lower number of cases among Hindus may be due to the declining trend of the disease among the Hindus due to better awareness. This study shows slightly higher prevalence of disease among females compared to earlier studies. This suggests the changing trend of the epidemiology of AIDS where the disease is affecting the most vulnerable segment of the society. According to Manipur AIDS Control Society (MACS) the ratio of male to female is 2.7 : 1.⁶ This study also reflects the changing trend of the disease transmission where sexual spread is becoming the major route. This may be due to needle syringe exchange programme taken up by MACS, NACO and also may be due to the small study group among hospitalized severe AIDS cases. Mean age in this study was 38.5 years. According to MACS the maximum number of cases is seen in the age group of 20 – 30 yrs.⁷ The higher age group contributing to the maximum number of cases in this study may be due to the fact that the HIV/AIDS patients are surviving for a longer period with the advent of newer antiretroviral therapy. According to the annual report of Government of India, majority of the HIV infection are seen in the age group of 15 – 49 years comprising of 88.55%, out of which 31.8% cases are seen in the age group of 15 – 29 years.⁸ Total number of cases coinfecting with HIV, HBV and HCV

were 14(28%); four cases of HBV, nine cases of HCV and one combined HBV and HCV. According to Saha M K et al 92% of the HIV positive patients with history of IVDU were infected with HCV and HBV was seen in 100% of the cases.⁹ Since the introduction of HAART the AIDS related mortality has decreased and end stage liver disease has become a leading cause of death in the HIV infected patients. In another study by Johann O et al ('97) the prevalence of HBV and HCV was 9% and 23% respectively.¹⁰ In a study by De et al in 2002 the prevalence was 6.8% and 45.5% respectively.¹¹ Mathur et al in 2002 found a prevalence of 6.1% and 26.7% respectively.¹²

In this study Cryptococcal meningitis was seen in four (8%) cases and mean CD₄ count was 37.5 cells/ μ L. In all these cases CD₄ count were <50/ μ L. Cryptococcosis is the most common CNS fungal infection AIDS patients and the 3rd most common infection involving brain.³ M Fernandez reported that 84% of the patients with cryptococcosis had CD₄ count <200/ μ L.¹³ V Lakshmi in her study found that Cryptococcal meningitis increases with declining CD₄ count and highest risk was seen with CD₄ count <50/ μ L.¹⁴

Progressive multifocal leukoencephalopathy and toxoplasmosis were seen when CD₄ count was less than 100 cells/ μ L. In this study PML was seen in 7 (14%) cases and is the 4th most common neurological disease among AIDS patients. Prevalence of PML in AIDS patients is reported to be 5 -7%³. Mean CD₄ count was 88.5 cells/ μ L. Two of the PML cases had involvement of cerebellum and was the first presentation of AIDS. In a study by Berger J R et al the prevalence of PML in AIDS patients was 3.8%¹⁵. In another study by Vazeux R et al the prevalence was 6%.¹⁶ Von Einsiedel RW et al found a mean CD₄ count of 84/ μ L in PML patients.¹⁷

Toxoplasmosis was seen in 4 (8%) cases with mean CD₄ count was 56.25/ μ L. In 50% cases it is AIDS defining illness. Del Rio Chiriboga C et al (97) reported that CD₄ count < 100 cells/ μ L was associated with toxoplasmosis.¹⁸ In another study by Berger and Levy ('93) toxoplasmosis was the commonest opportunistic infection in AIDS patients.¹⁹ In another study by Jay CA (2000) toxoplasmosis was seen in 5 - 10% of the patients with AIDS.²⁰ Racial and geographical susceptibility to toxoplasma infection also occurs. Single positive IgG titre is a sensitive indicator of prior infection. Raised or rising titre do not necessary indicate active infection and < 5% of the cases have negative serology.³

The commonest neurological disease associated with AIDS was CNS tuberculosis comprising 10(20%) of the cases with a mean CD₄ count of 122/ μ L. Out of 10 cases of CNS tuberculosis 7 (70%) had CD₄ count >100 cells/ μ L. In India 28-30% of TB patients are HIV positive and 5 - 9% of AIDS patients have TB. CNS TB is seen in 2 -5% of all patients with TB and 10% of AIDS related TB has CNS TB.²⁰ The spectrum of CNS tuberculosis in this study include tubercular meningitis (3, 30%), abscess(2, 20%), focal cerebritis(1, 10%), and tuberculoma(4, 40%). In a study by Berenguer et al ('92) the prevalence of tuberculosis in AIDS patients was 59%.²¹ Torok et al (2008) found a median CD₄ count of 32 cells/ μ L in cases of TBM.²² Berger J et al (1993) mentioned that CD₄ count of < 200 cells/ μ L was associated

with a poor prognosis.¹⁹ TBM was the commonest type of meningitis associated with HIV transmission by intravenous drug abuse.²³

CMV encephalitis was seen in 4 (8%) cases in this study. This was 5th most common disease among the AIDS patients in this study. Mean CD₄ count in cases of CMV encephalitis was 104/ μ L. Prevalence of cytomegalovirus encephalitis was reported to be 15 - 30% in AIDS patients.¹ This is seen mainly in cases where CD₄ count is <100/ μ L.² Slightly higher CD₄ count in these cases may be due to the fact that these patients were on ART for a variable period.

In this study HIV encephalitis was seen in 9 (18%) cases. This was the 2nd most common disease in this study. Mean CD₄ count was 183.3/ μ L. HIV encephalitis is reported as the most common CNS manifestation of HIV/AIDS. Jowi J O reported that mean CD₄ count in HIV encephalitis was 82/ μ L.²⁴ Wong et al reported mean CD₄ count of <100/ μ L in cases with HIV dementia complex.²⁵

Cerebral infarction was seen in eight (16%) of the cases. This was the 3rd most common disease in this study. Mean CD₄ count was 238.5/ μ L. Out of these 8 cases basal ganglia was involved in six (6) cases and in two (2) cases cerebral hemispheres were involved. Ortiz G (2007) reported mean CD₄ count of 113 cells/ μ L in patients of cerebral infarction associated with AIDS.²⁶ This pattern of CNS complication of AIDS is suggested to be due to vasculitis, thrombosis, direct effect of the virus.

HIV demyelination was seen in one case only. This was least common disease in this study. This is seen in rarely in AIDS patients. CD₄ count in this patient was 89 cells / μ L.

Fisher's exact test was performed on this dataset using the SPSS Software Version 15 and the taking the significance level as 0.01 the Fisher exact test statistical value is 0.001164. The result is significant at p < 0.01. Thus CD4+ count has a very strong correlation with occurrence of opportunistic infections.

CONCLUSION

MRI of brain is helps in early diagnosis and treatment in AIDS patients, increasing the life span of these patients with significant reduction in mortality and morbidity. MRI has high sensitivity and specificity in diagnosis of various brain lesions in patients with AIDS and detects the lesions when the patient may be clinically asymptomatic and serological tests are negative. This study shows few important epidemiological findings - increasing prevalence among females, increasing sexual transmission, CNS tuberculosis commoner than toxoplasmosis and slightly higher mean CD4+ count in different opportunistic infections compared to the pre ART era.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 09-03-2021; **Accepted:** 30-03-2021; **Published online:** 04-04-2021