

**TITLE PAGE:**

**EVALUATION OF CNS MANIFESTATIONS IN HIV  
PATIENTS ON MRI BRAIN STUDY**

- 1. Dr Amol Ramkishan Musale**, Assistant professor, Department of Radiodiagnosis, BJ GMC & SGH, Pune.
- 2. Dr Vishal Walasangikar**, Assistant professor, Department of Radiodiagnosis, BJ GMC & SGH, Pune. Corresponding author. vishalwalasangikar@gmail.com, contact number: 9405641046. Orchid id: 0000-0002-4798-8904. Address for communication : Flat no 202, Ghar heights, near Rudreshwar chowk, LIC colony, Latur, Maharashtra, India.
- 3. Dr Sneha Gaikwad**, Junior resident, Department of Radiodiagnosis, BJ GMC & SGH, Pune. Gsneha44@gmail.com

**ABSTRACT:**

**Background:** Infection by the human immunodeficiency virus (HIV) can lead to diverse clinical symptoms. As HIV comes under lentivirus category, they are capable of producing chronic neurologic damage to its animal host. Transmigration of HIV-infected CD4+ cells across the blood-brain barrier causes the infection to the resident cells of central nervous system (CNS).<sup>1,2</sup> Imaging technologies play an important role in guiding accurate diagnosis and proper therapy in neuronal complications induced by HIV. Impact of HIV in the CNS can be well assessed by magnetic resonance imaging (MRI). MRI can favorably show the range and depth of soft tissue infections, and necrosis and has a higher sensitivity to pick up new lesions; hence making it the modality of choice.

**Aim & Objective:** **1.** To evaluate spectrum of imaging findings in asymptomatic and symptomatic HIV positive patients. **2.** Classify and characterize the lesions on MRI imaging. **3.** To correlate the MRI findings clinically with CD 4 count

**Study design:** Prospective study

**Study setting:** Radiology Department of tertiary care centre

**Study duration:** 2 years (October 2020 to December 2021).

**Study population:** Definitive diagnosis of HIV cases referred to Department of Radiodiagnosis for brain MRI such cases were included for study. **Sample size:** 80

**Results:** Majority of the patients (55%) were in the age group of 29 to 38 years followed by 21% patients were in the age group of 39 to 48 years with least i.e 1.25% patients in the age group 59 to 68 years. There was male predominance (72.5%), whereas female patients constituted 27.5% of the study group. Amongst 80 seropositive cases 32 were diagnosed with Cerebral Tuberculosis, 10 were diagnosed with toxoplasmosis, 11 were diagnosed with Encephalitis/ Dementia, 7 were diagnosed with PML, 5 with cryptococcal meningitis, 4 with lymphoma, 2 with pyogenic infection, 2 with cerebrovascular disease, 1 with CMV and 1 with HSV encephalitis. Amongst 80 seropositive cases symptoms were present in 73 whereas asymptomatic cases were 7. correlation of MRI with occurrence of Symptoms. Amongst 73

symptomatic cases all were found abnormality on MRI whereas amongst 7 asymptomatic cases 3 were shows abnormality on MRI and 4 were normal. In patients with cerebral tuberculosis mean CD4 count was 131, in patients with Toxoplasmosis mean CD4 count was 75.88, in patients with HIV Encephalitis/ Dementia mean CD4 count was 208.44, in patients with Cryptococcal Meningitis mean CD4 count was 96.50, in patients with CMV mean CD4 count was 64.00, in patients with Lymphoma mean CD4 count was 88.00, in patients with PML mean CD4 count was 87.33, in patients with Pyogenic Infections/Abscess mean CD4 count was 68.00, in patients with Cerebrovascular Disease mean CD4 count was 226.00, in patients with HSV Encephalitis mean CD4 count was 58.00 and amongst seropositive patients with no abnormality mean CD4 count was 235.00

**Conclusions:** Most affected age group is 3<sup>rd</sup> and 4<sup>th</sup> decade with male preponderance. Majority of the patients presented with symptoms had positive imaging finding. Cerebral tuberculosis is the most common pathology encountered presented with meningitis. RI with diffusion weighted imaging and spectroscopy is the modality of choice. There is no correlation between CD4 count and pathology.

Keywords: MRI, HIV, CNS, Infection, tuberculosis, Cryptococcosis, lymphoma.

## INTRODUCTION:

Infection by the human immunodeficiency virus (HIV) can lead to diverse clinical symptoms. As HIV comes under lentivirus category, they are capable of producing chronic neurologic damage to its animal host. Transmigration of HIV-infected CD4+ cells across the blood-brain barrier causes the infection to the resident cells of central nervous system (CNS).<sup>1,2</sup>

HIV-associated CNS abnormalities can be mainly in the form of lesions, infections, and neoplasms. It may represent as neurocognitive disorders, neuropathy, lymphomas, dementia, vacuolar myelopathy, psychological conditions, and neurological opportunistic infections. Opportunistic infections are one of the major causes that exacerbate the condition of HIV-infected patients with high level of morbidity and mortality rate. These include leukoencephalopathy, toxoplasmosis, cryptococcal meningitis, tuberculosis, neurosyphilis.<sup>3,4</sup>

Imaging technologies play an important role in guiding accurate diagnosis and proper therapy in neuronal complications induced by HIV. Impact of HIV in the CNS can be well assessed by magnetic resonance imaging (MRI). MRI can favorably show the range and depth of soft tissue infections, and necrosis and has a higher sensitivity to pick up new lesions; hence making it the modality of choice. It helps to understand the pathological process and disease progression, non-invasively.<sup>5,6</sup> Therefore, in the present study, MRI was used to differentiate and characterize the brain lesions in the HIV-infected patients.

## METHODOLOGY:

**Study design:** Prospective study, **Study setting:** Radiology department of tertiary care centre

**Study duration:** 2 years (from October 2020 to December 2021), **Study population:** definitive diagnosis of HIV cases referred to Department of Radio-Diagnosis for brain MRI such cases were included for study.

**SAMPLE SIZE:** 80

**Inclusion criteria:**

1. All definitive diagnosis of HIV cases referred to Department of Radio-Diagnosis for brain MRI such cases were included for study.

**Exclusion criteria:**

1. Not willing to participate. 2. Loss to follow-up.

**Approval for the study:** Written approval from Institutional Ethics committee was obtained beforehand. Written approval of Radiology department was obtained. After obtaining informed verbal consent from all patients with the definitive diagnosis of HIV cases referred to Department of Radio-Diagnosis for brain MRI such cases were included for study.

**Sampling technique:** Total population sampling technique used for data collection. All patients admitted in Radiology department of tertiary care center from Jan 2020 to Dec 2021 definitive diagnosis of HIV cases referred to Department of Radio-Diagnosis for brain MRI such cases were included for study. Explained the purpose of study and who gave consent and detailed history

**Methods of Data Collection and Questionnaire-** Predesigned and pretested questionnaire was used to record the necessary information. Questionnaires included general information, such as age, sex, religion, occupation of parents, residential address, socioeconomic status and date of admission. The study included 80 patients diagnosed as HIV-positive by enzyme-linked immunosorbent assay referred to the Department of Radio-Diagnosis for brain MRI. Patients those fulfilled the selection criteria were informed about the nature and purpose of the study and were enrolled after obtaining a written informed consent. Patients with ferromagnetic implants, pacemakers and aneurysm clips and those without any visualized MRI pathology were excluded from the study.

**Imaging procedure:** Brain MRI of all patients was carried out using 1.5 Tesla Symphony Maestro class-MRI with the help of a dedicated brain coil. The test was performed using a field of view of 230-mm, slice thickness of 4 mm and matrix size of 256 ×256 mm. Spin-echo T1 and T2-weighted (axial/sagittal), fluid attenuated inversion recovery (axial), diffusion-weighted imaging (DWI), and gadolinium-enhanced fat-suppressed T1-weighted sequences were obtained. Susceptibility weighted imaging and magnetic resonance spectroscopy sequences of the brain were obtained in required cases. The collected data were expressed as proportions and percentages as per the suitability

**RESULTS AND OBSERVATIONS:**

Majority of the patients (55%) were in the age group of 29 to 38 years followed by 21% patients were in the age group of 39 to 48 years with least i.e 1.25% patients in the age group 59 to 68 years. There was male predominance (72.5%), whereas female patients constituted 27.5% of the study group.

**Table no.1 Distribution of cases according to Cerebral Abnormality**

<b>Sr. No.</b>	<b>Cerebral Abnormality in Seropositive Patients</b>	<b>No. of Cases N</b>	<b>Percentage %</b>
<b>1</b>	Cerebral Tuberculosis	32	40 %
<b>2</b>	Toxoplasmosis	10	12.5 %
<b>3</b>	HIV Encephalitis/ Dementia	11	13.75 %
<b>4</b>	Cryptococcal Meningitis	5	6.25 %
<b>5</b>	CMV	1	1.25 %
<b>6</b>	Lymphoma	4	5 %
<b>7</b>	PML	7	8.75 %
<b>8</b>	Pyogenic Infections/Abcess	2	2.5 %
<b>9</b>	Cerebrovascular Disease	2	2.5 %
<b>10</b>	HSV Encephalitis	1	1.25 %
<b>11</b>	No Abnormality	5	6.25 %
<b>Total</b>		<b>80</b>	<b>100 %</b>

The above table no 1 shows Distribution of cases according to Cerebral Abnormality in Seropositive Patients. Amongst 80 seropositive cases 32 were diagnosed with Cerebral Tuberculosis, 10 were diagnosed with toxoplasmosis, 11 were diagnosed with Encephalitis/ Dementia, 7 were diagnosed with PML, 5 with cryptococcal meningitis, 4 with lymphoma, 2 with pyogenic infection, 2 with cerebrovascular disease, 1 with CMV and 1 with HSV encephalitis

**Table 2: Distribution of cases according to occurrence of Symptoms**

<b>Sr. No.</b>	<b>Occurrence of Symptoms</b>	<b>No. of Cases N</b>	<b>Percentage %</b>
<b>1</b>	Asymptomatic	7	8.75
<b>2</b>	Present	73	91.25
<b>Total</b>		<b>80</b>	<b>100 %</b>

**Table 2** shows distribution of cases according to occurrence of Symptoms. Amongst 80 seropositive cases symptoms were present in 73 whereas asymptomatic cases were 7

**Table 3: Association of MRI with occurrence of Symptoms**

Sr. No.	Occurrence of Symptoms	MRI		Total
		Normal n (%)	Abnormal n (%)	
1	Asymptomatic	4 (5 %)	3 (4 %)	7 (9 %)
2	Present	0 (0 %)	73 (91 %)	73 (91.25 %)
<b>Total</b>		4 (5 %)	76 (95 %)	80 (100 %)

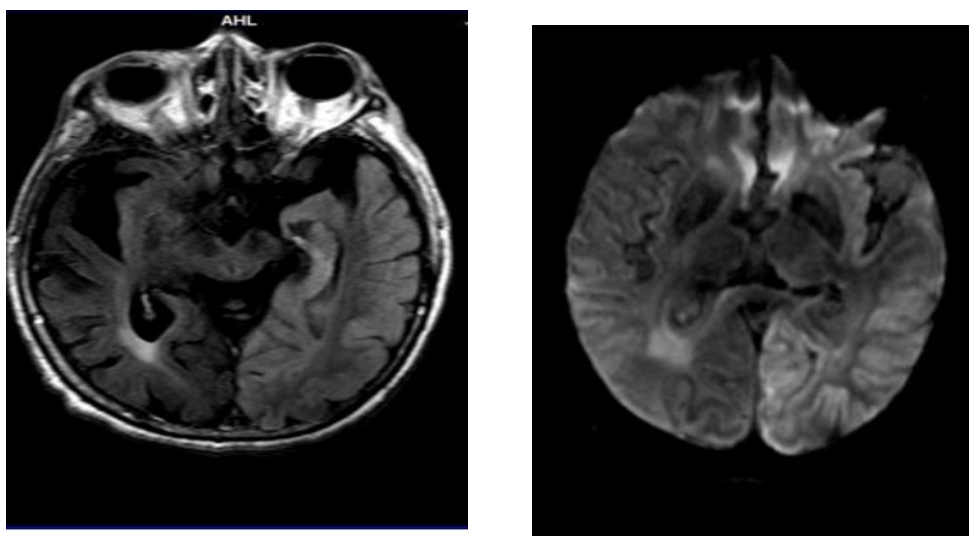
**Table 3** shows correlation of MRI with occurrence of Symptoms. Amongst 73 symptomatic cases all were found abnormality on MRI whereas amongst 7 asymptomatic cases 3 were shows abnormality on MRI and 4 were normal

**Table 4: Distribution of cases according to CD4 count**

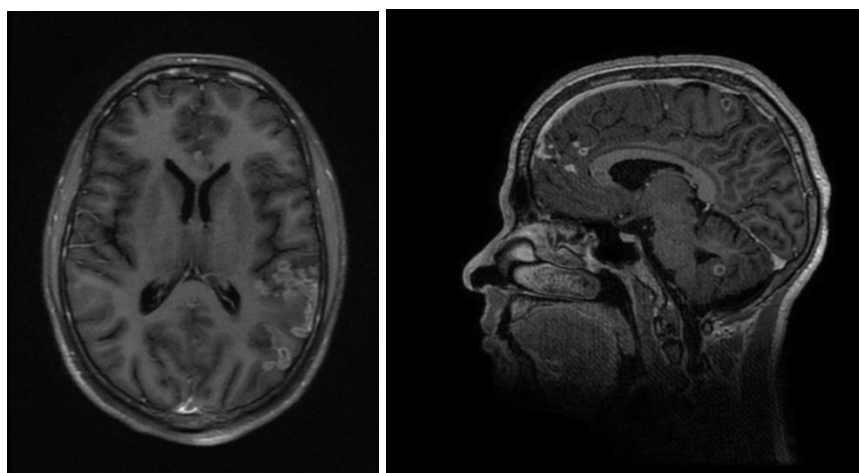
Cerebral Abnormality in Seropositive Patients	No. of Cases N	Mean	SD	SEM	Median	25 %	75 %
Cerebral Tuberculosis	32	131.00	65.65	20.76	115.00	90.00	140.00
Toxoplasmosis	10	75.88	29.82	10.54	75.00	61.50	102.00
HIV Encephalitis/ Dementia	11	208.44	22.93	7.64	206.00	188.50	222.50
Cryptococcal Meningitis	5	96.50	22.71	11.35	98.00	78.00	115.00
CMV	1	64.00	0.00	0.00	64.00	64.00	64.00
Lymphoma	4	88.00	54.15	31.26	64.00	53.50	128.50
PML	7	87.33	18.27	7.46	86.00	70.00	104.00
Pyogenic Infections/Abcess	3	68.00	0.00	0.00	68.00	68.00	68.00

Cerebrovascular Disease	2	226.00	0.00	0.00	226.00	226.00	226.00
HSV Encephalitis	1	58.00	0.00	0.00	58.00	58.00	58.00
No Abnormality	4	235.00	49.50	35.00	235.00	200.00	270.00

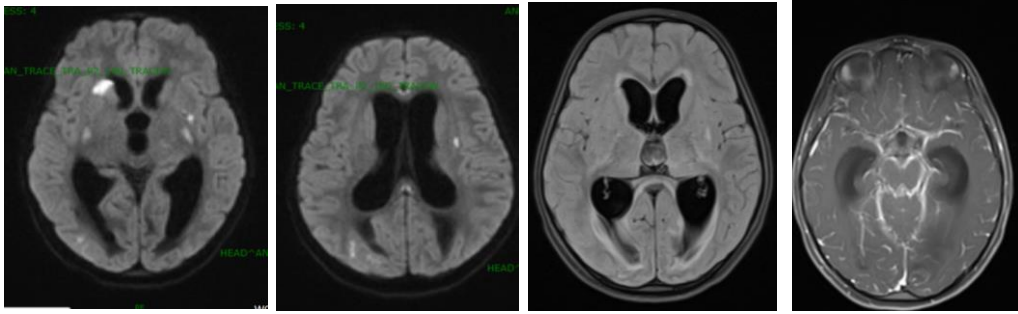
**Table 4** shows distribution of cases according to CD4 count. In patients with cerebral tuberculosis mean CD4 count was 131, in patients with Toxoplasmosis mean CD4 count was 75.88, in patients with HIV Encephalitis/ Dementia mean CD4 count was 208.44, in patients with Cryptococcal Meningitis mean CD4 count was 96.50, in patients with CMV mean CD4 count was 64.00, in patients with Lymphoma mean CD4 count was 88.00, in patients with PML mean CD4 count was 87.33, in patients with Pyogenic Infections/Abscess mean CD4 count was 68.00, in patients with Cerebrovascular Disease mean CD4 count was 226.00, in patients with HSV Encephalitis mean CD4 count was 58.00 and amongst seropositive patients with no abnormality mean CD4 count was 235.00.



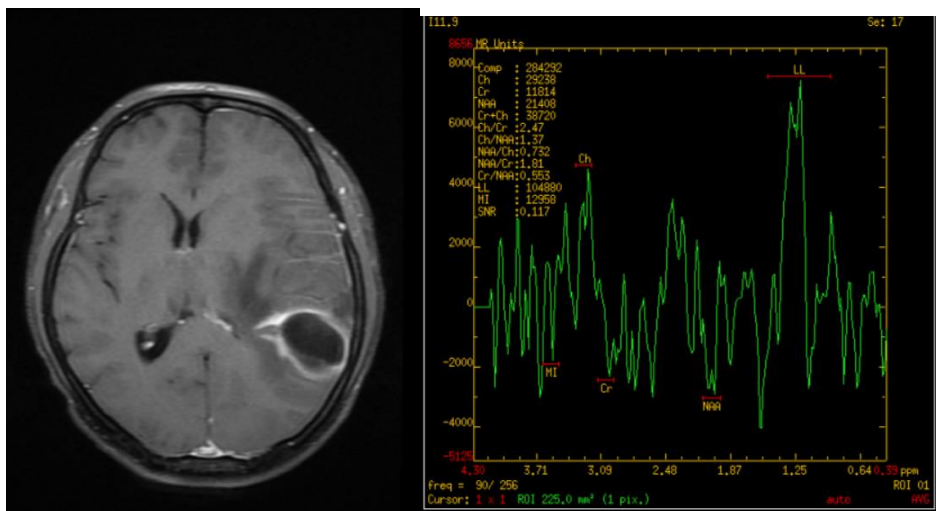
**Fig;1 a) Axial FLAIR b) Axial DWI images in patients with herpes encephalitis shows cortical and subcortical hyperintensity involving the left temporal lobe cortex with diffusion restriction.**



**Fig;2 a) Axial post contrast T1 FAT SAT b) Saggital post contrast T1 FAT SAT images of tuberculomas showing multiple conglomerated ring enhancing lesions involving fronto-parito-occipital region and cerebellum.**

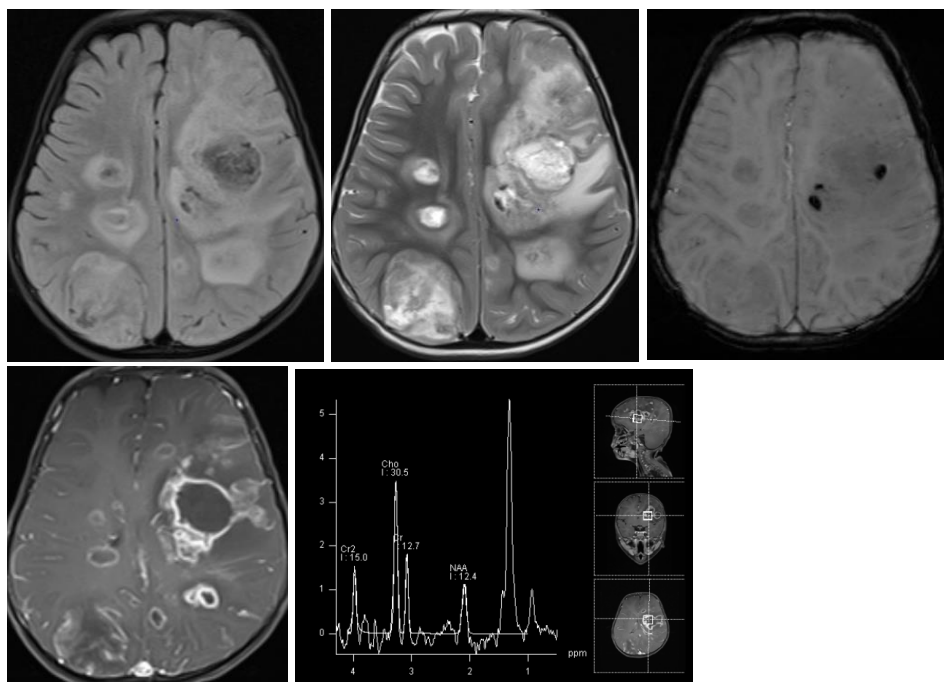


**Fig;3 a) Axial DWI b) Axial DWI c) Axial FLAIR d) Axial post contrast FAT SAT T1W images in patients with tubercular meningitis, shows vasculitis infarcts in both gangliocapsular regions, periventricular white matter with hydrocephalus and diffuse leptomeningitis.**

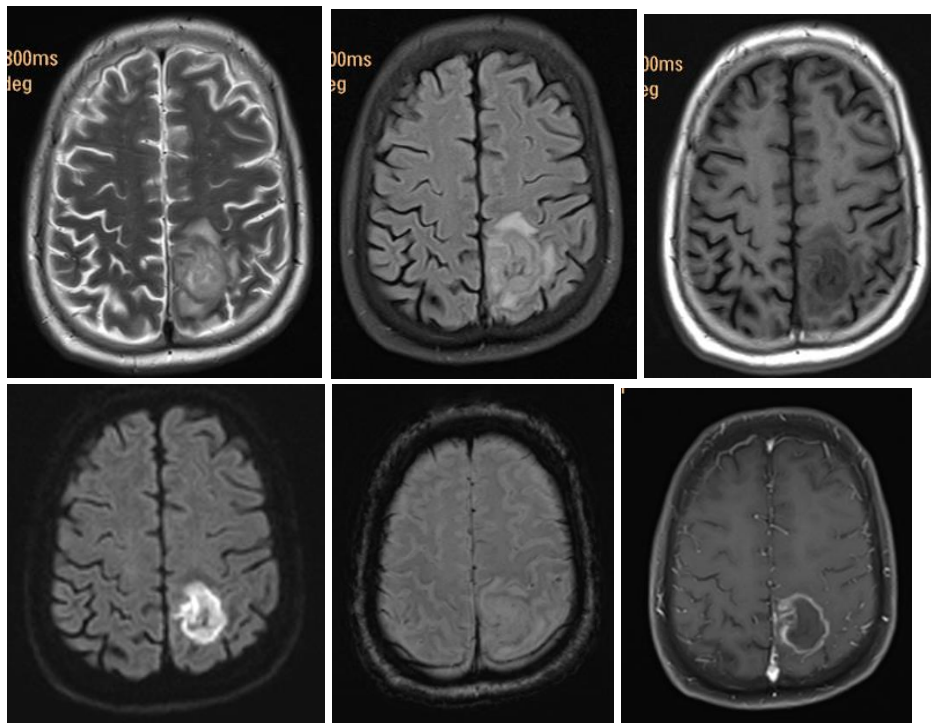


**Fig ;4 a) Axial postcontrast b) MRS in a patient of cerebral abscess showing ring enhancing lesion involving cortical and subcortical white matter of left parietal lobe with mass effect. MRS shows lipid lactate peak.**

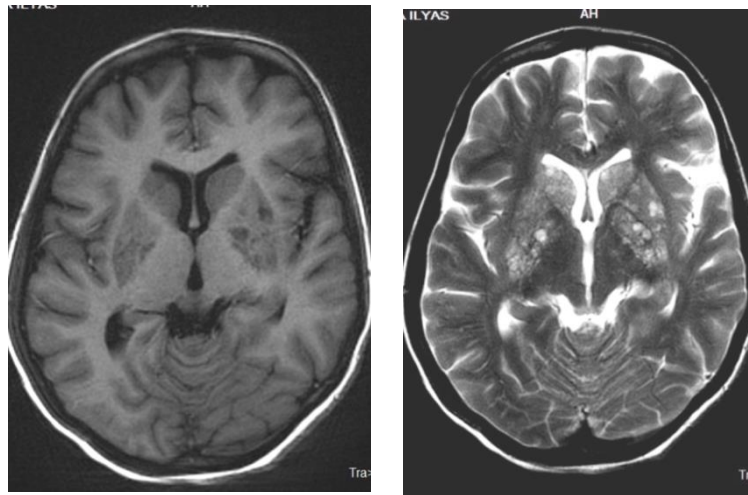




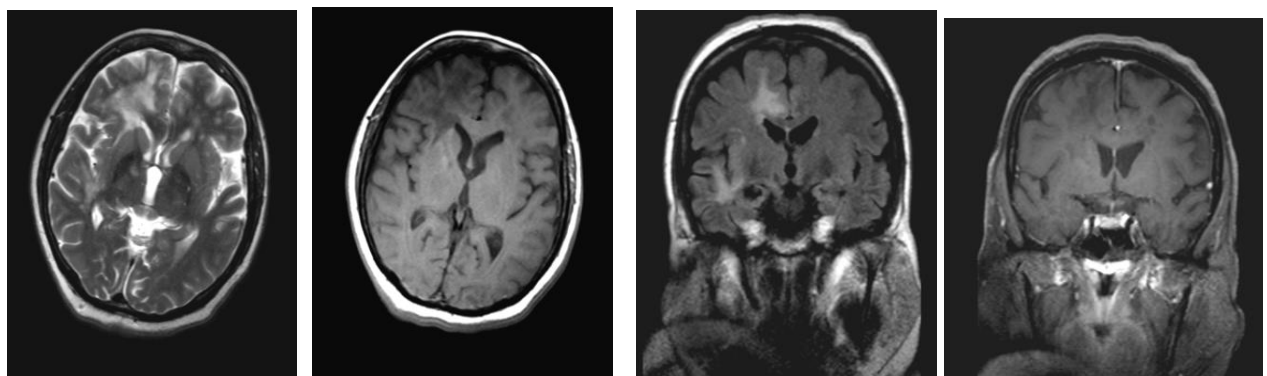
**Fig;5 a) Axial FLAIR b) Axial T2W c) SWI d) Axial post contrast FAT SAT T1W e) single voxel spectroscopy images in patients with fungal infection shows multiple ring enhancing lesions involving both cerebral hemispheres with raised lipid lactate and choline peak.**



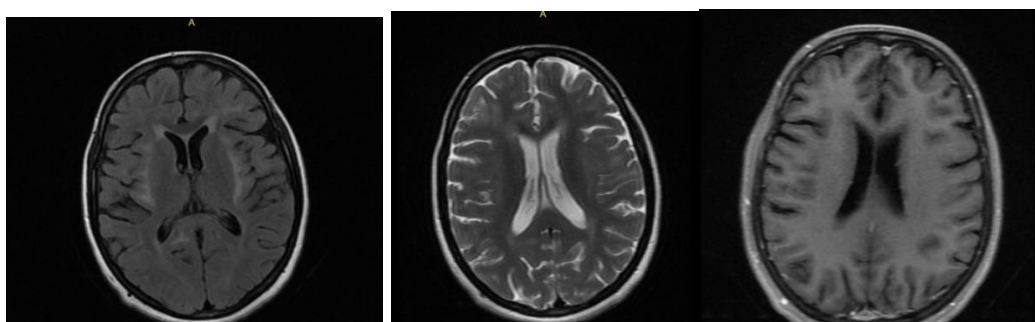
**Fig;4 a) Axial T2W b) Axial FLAIR c) T1W d) DWI e) SWI f) Axial post contrast FAT SAT T1W images in patients with toxoplasma infection shows ring enhancing lesion in left parietal lobe.**



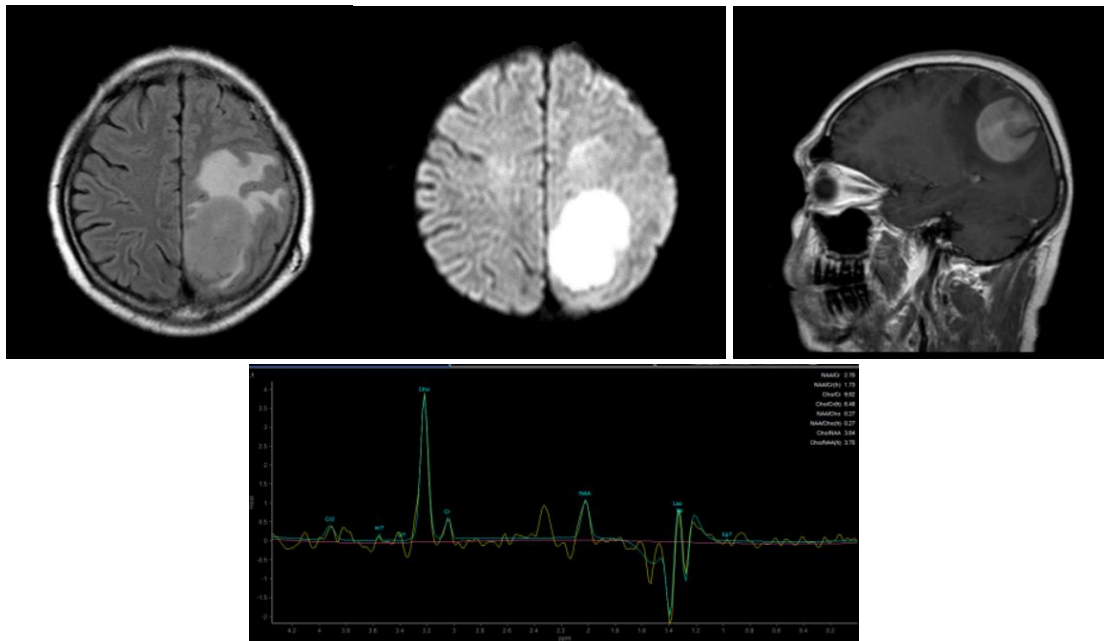
**Fig;5 a) Axial T1W b) Axial T2W images in patient with Cryptococcus reveals, small non-enhancing hypodensities typically within the basal ganglia representing dilated perivascular spaces.**



**Fig;6 a) Axial T2WI b) T1WI c) Axial FLAIR d) PC T1W FAT SAT images in a patient with PML. Patchy areas of low T1 signal and high T2 signal in the subcortical frontal and periventricular white matter with no post-contrast enhancement.**



**Fig;7 a) Axial FLAIR b) Axial T2WI c) T1W FAT SAT Post Contrast images of a patient with HIV encephalopathy. The images demonstrate high signal intensity is seen in the periventricular white matter of the frontal and parieto-occipital regions with no post contrast enhancement.**



**Fig;8 a) Axial FLAIR b) Axial DWI c) Saggital T1W FAT SAT post contrast d) MRS of a patient of lymphoma.FLAIR hyperintense lesion with perilesional edema noted in subcortical white matter of left parietal lobe,restriction on DWI with homogenous post contrast enhancement.MRS shows choline peak.**

#### DISCUSSION:

In present study Distribution of cases according to Cerebral Abnormality in Seropositive Patients. Amongst 80 seropositive cases 32 were diagnosed with Cerebral Tuberculosis, 10 were diagnosed with toxoplasmosis, 11 were diagnosed with Encephalitis/ Dementia, 7 were diagnosed with PML, 5 with cryptococcal meningitis, 4 with lymphoma, 2 with pyogenic infection, 2 with cerebrovascular disease, 1 with CMV and 1 with HSV encephalitis. Similar observations were found in the study conducted by Ramírez-Crescencio et al.<sup>7</sup> and Mohraz M et al.<sup>8</sup>

In present study Amongst 80 seropositive cases symptoms were present in 73 whereas asymptomatic cases were 7. Similar result found in the study by Rohan Bhanushali et al.<sup>9</sup>

In present study correlation of MRI with occurrence of Symptoms. Amongst 73 symptomatic cases all were found abnormality on MRI whereas amongst 7 asymptomatic cases 3 were shows abnormality on MRI and 4 were normal. Similar result observed in the study by Saini S et al.<sup>10</sup>

In present study distribution of cases according to CD4 count. In patients with cerebral tuberculosis mean CD4 count was 131, in patients with Toxoplasmosis mean CD4 count was 75.88, in patients with HIV Encephalitis/ Dementia mean CD4 count was 208.44, in patients with Cryptococcal Meningitis mean CD4 count was 96.50, in patients with CMV mean CD4 count was 64.00, in patients with Lymphoma mean CD4 count was 88.00, in patients with PML mean CD4 count was 87.33, in patients with Pyogenic Infections/Abscess mean CD4

count was 68.00, in patients with Cerebrovascular Disease mean CD4 count was 226.00, in patients with HSV Encephalitis mean CD4 count was 58.00 and amongst seropositive patients with no abnormality mean CD4 count was 235.00. similar result found in the study by García AI et al.

**CONCLUSIONS:** Most affected age group is 3<sup>rd</sup> and 4<sup>th</sup> decade with male preponderance. 91% the patients were symptomatic and were having positive imaging findings. Cerebral tuberculosis is the most common pathology encountered presented as meningitis. MRI with diffusion weighted imaging and spectroscopy is the modality of choice. There is no correlation between CD4 count and prevalence of specific pathology.

### References:

1. Atluri VS, Hidalgo M, Samikkannu T, et al. Effect of human immunodeficiency virus on blood-brain barrier integrity and function: an update. *Front Cell Neurosci.* 2015;9(1):212.
2. Hazleton JE, Berman JW, Eugenin EA. Novel mechanisms of central nervous system damage in HIV infection. *HIV AIDS (Auckl).* 2010;2(5):39-49.
3. Le LT, Spudich SS. HIV-Associated Neurologic Disorders and Central Nervous System Opportunistic Infections in HIV. *Semin Neurol.* 2016;36(4):373-81.
4. Kranick SM, Nath A. Neurologic complications of HIV-1 infection and its treatment in the era of antiretroviral therapy. *Continuum.* 2012;18(6 Infectious Disease):1319-37.
5. Tate DF, Khedraki R, McCaffrey D, et al. The role of medical imaging in defining CNS abnormalities associated with HIV-infection and opportunistic infections. *Neurotherapeutics.* 2011;8(1):103-16.
6. Zhao F, Sun L-q, Tian Y-m, et al. The diagnostic value of brain magnetic resonance imaging in detecting CNS diseases among advanced AIDS patients. *Infection International.* 2014;3(4):173-8
7. Ramirez-Crescencio MA, Velasquez-Perez L, RamirezCrescencio MA, et al. Epidemiology and trend of neurological diseases associated to HIV/AIDS. Experience of Mexican patients 1995-2009. *Clin Neurol Neurosurg.* 2013;115(8):1322-5.
8. Mohraz M, Jozani ZB, Behtaj M, et al. Neurological manifestations in HIV positive patients in Tehran, Iran. *Asian Pac J Trop Dis.* 2014;4(4):S481-S5.
9. Rohan Bhanushali, Pradeepgoud H. Patil. Role of magnetic resonance imaging in evaluation of the brain lesions in HIV-infected patients: a prospective observational study. *International Journal of Contemporary Medicine Surgery and Radiology.* 2019;4(3):C34-C37
10. . Saini S, Barar KV. Assessment of neurocognitive functions in HIV/AIDS patients on HAART using the international HIV dementia scale. *Int J Nutr Pharmacol Neurol Dis.* 2014;4(4):252.
11. García AI, Milinkovic A, Tomás X, Rios J, Pérez I, Vidal-Sicart S, Pomés J, Del Amo M, Mallolas J. MRI signal changes of the bone marrow in HIV-infected patients with lipodystrophy: correlation with clinical parameters. *Skeletal Radiol.* 2011

Oct;40(10):1295-301. doi: 10.1007/s00256-011-1147-x. Epub 2011 Apr 10. PMID: 21479859.