

Original Research Article

## Radiological Abnormalities in HIV Infected Patients with Neurologic Symptoms and Diagnostic Accuracy of CT and MRI Scans of Brain

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### ABSTRACT

**Introduction:** Prevalence of HIV infection is high in India with neurological complications developing in many patients. CT scan and MRI are helpful in identifying the neurological abnormalities in such patients. This study aims to find prevalence of various neurological abnormalities in HIV infected patients with clinical evidence of neurological involvement in a tertiary care center and to assess the accuracy of CT scan and MRI in their evaluation.

**Materials and Methods:** This was a cross sectional observational study done in Department of Radiodiagnosis, for one year and six months. HIV positive patients having neurological symptoms referred for CT scan or MRI scan of brain were included. CT scan was taken for 54 patients and MRI for 48 patients. Presumed diagnosis was made from radiological diagnosis, history, clinical and laboratory data, based on which the patients were treated. Patients were then followed up for final diagnosis made from medical records, based on history, neurological examination, further imaging, laboratory data and treatment response. We correlated the radiological diagnosis from CT scan and MRI with the final diagnosis. Sensitivity, specificity, positive predictive value and negative predictive value for CT scan and MRI were calculated.

**Results & Conclusion:** HIV encephalopathy (n=8), toxoplasmosis (n=6), infarcts and tuberculosis (n=5 each) accounted for most neurological abnormalities. MRI was much more sensitive and specific than CT scan. CT scan could predict final diagnosis in 38 out of 54 cases (70.37% sensitivity) while MRI could predict final diagnosis in 43 out of 48 patients (89.58% sensitivity)

**Keywords:** HIV; neurological; computed tomography; magnetic resonance imaging.

### Introduction

In India, the prevalence of human immunodeficiency virus (HIV) infection is high, possibly

due to increased prevalence of sexually transmitted diseases, poverty and illiteracy. HIV remains a major public health threat with about 21.17 lakh

people living with HIV in India in 2015 <sup>[1]</sup>. The HIV is a retrovirus which predominantly infects cells of the immune system disrupting their function. It is a neurotropic virus and neurological manifestations are seen in a significant percentage of patients with HIV <sup>[2]</sup>. HIV can affect central nervous system in different ways. This can either be due to HIV virus itself by infecting the macrophages in central nervous system (CNS) or due to neoplasms and by the activity of other opportunistic pathogens which takes the advantage of development of progressive immunodeficiency <sup>[3]</sup>. During the course of the illness neurological symptoms are seen in about 40% of HIV infected patients. Neurological disease is the presenting manifestation of 10-20% of patients with acquired immunodeficiency syndrome (AIDS). With the prolongation of survival in HIV-positive persons, CNS abnormalities are increasingly seen. Development of neurological abnormalities increases the morbidity and mortality in HIV infected persons. A high index of clinical suspicion of neurological involvement in patients with HIV helps in prompt diagnosis and early treatment, which in turn reduces morbidity and mortality significantly

Hence the knowledge of CNS manifestations in HIV patients is very important for proper diagnosis and management. CT scan is the most easily available imaging tool in evaluation of neurological abnormalities, when compared to MRI. In this study, we aim to find the prevalence of various neurological abnormalities in HIV patients with clinical evidence of neurological involvement in a tertiary center in South India and to assess the accuracy of CT scan and MRI in their evaluation.

### Materials and Methods

The study was a cross sectional observational study done in department of Radiodiagnosis for a period of one year and six months, from January 2013 to June 2014. HIV positive persons registered in antiretroviral therapy (ART) clinic having neurological symptoms like persistent head ache (more than 1 week), seizures, focal neurological

deficits or altered mental status and referred to department of Radiodiagnosis for CT scan or MRI scan of head were included in the study. Persons who were already known cases of neurological disease before detection of HIV positive status were excluded from the study. Patients who were not followed up in our hospital for final diagnosis were also excluded.

There were a total of 67 HIV infected patients referred for CT or MRI scan of head of which 11 cases were excluded as they were follow up cases for known neurologic disorder and 2 cases lost follow up as they were transferred out to another ART center. Remaining 54 patients were included in the study. CT scan of head was taken for all these 54 patients while MRI was done only in 48 patients. Persons who were found to be normal on CT, had symptomatic relief with medication and not willing for MRI evaluation were not considered for MRI. The study was conducted with informed consent from the patients after getting permission from Ethical committee. CT and MRI images were assessed by a radiologist and a resident in radiology. Radiological diagnosis were made using standard references. Presumed diagnosis was made from radiological diagnosis, history and clinical and laboratory data, based on which the patients were treated. Positive laboratory data includes serology, cerebrospinal fluid (CSF) cytology, CSF culture, CSF specific antigen for cryptococcus and CSF-PCR (polymerase chain reaction) for toxoplasma and cytomegalovirus (CMV). Patients were treated with specific medication based on the presumed diagnosis formulated from radiological and laboratory data. The treatment protocol was according to 2007 NACO guidelines for treatment and prevention of opportunistic infections. Patients were then followed up for final diagnosis. The final diagnosis is made from the medical records, based on history, neurological examination, further imaging, laboratory data, and treatment response (one or more method in each patient). CT scan and MRI diagnosis were correlated with the final diagnosis.

CT imaging was performed using Siemens Somatom Emotion – 16 CT scanner. Axial 1.2 mm pre contrast images were obtained from base of skull to vertex. Intravenous non-ionic iodinated contrast injection given and post contrast images were obtained in all patients who were not contraindicated by altered renal function or had previous history of hypersensitivity to iodinated contrast medium. Coronal and sagittal reformations were done. Images were examined using brain window and bone window settings. MRI was done using SignaHDxt 1.5Tesla machine by GE healthcare. Standard brain imaging included the following sequences. (Axial T1 Weighted and Axial, Coronal and Sagittal T2 Weighted, Coronal FLAIR, Coronal FSPGR, Axial Gradient echo, DWI and ADC sequences). Axial sections were taken parallel to corpus callosum. Post contrast T1 weighted axial and coronal images were taken after administration of intravenous paramagnetic contrast medium (Gadolinium chelates).

The data was entered in Microsoft Excel and descriptive statistics on the population of interest were generated from the data obtained. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for CT and MRI for various diseases taking final diagnosis as gold standard.

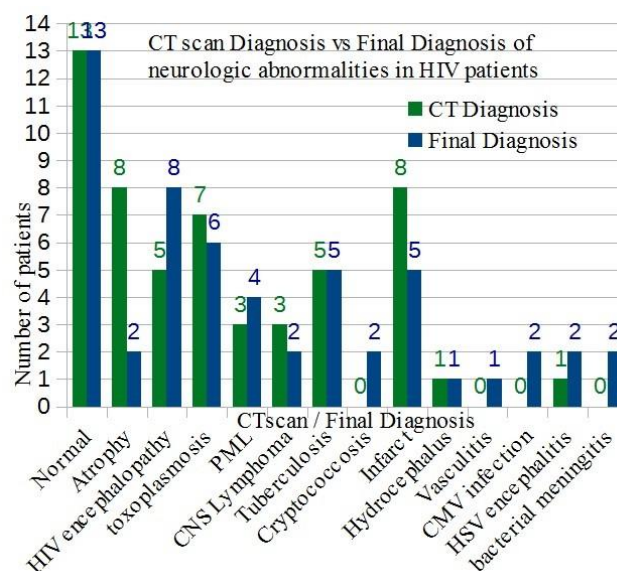
**Results**

Out of 54 persons included in the study, 33 (61%) were males and 21 (39%) were females. Most of them were in 30-39 years age group (n=4 in 0-9 years; n=1 in 10-19 years; n=6 in 20-29 years; n=21 in 30-39 years; n=16 in 40-49 years and n=6 in 50-59 years). Twenty eight persons (52%) were not on ART when CNS symptoms developed; neurological symptoms developed during ART in 26 persons (48%). At the end of the hospital stay, final diagnoses were: HIV encephalopathy (HIVE) in 8 cases; toxoplasmosis in 6 persons; CNS tuberculosis and infarct in 5 persons each; Progressive multifocal leukoencephalopathy (PMLE) in 4 persons, Atrophy, primary CNS lymphoma, cryptococcosis, cytomegalovirus (CMV) infection, bacterial

meningitis and Herpes simplex virus (HSV) encephalitis in 2 persons each and vasculopathy in 1 person. Thirteen persons were found to be having normal CNS after hospital work up and were kept in follow up. Thus the prevalence of neurological abnormalities in HIV infected patients with neurological symptoms was 75.93% (41 out of 54 patients)

Among the patients who underwent CT and MRI examinations, CNS abnormalities were identified in imaging studies only in 41 patients each. Among 54 cases who underwent CT scan, 13 had normal CT findings. The most common abnormalities identified in CT scan were atrophy and infarcts, seen in 14.81 % patients each (n= 8) followed by toxoplasmosis (12.96%, n=7), tuberculosis (9.26%, n=5) and HIVE (9.26%, n=5). [Figure 1] CT scan could correctly predict the final diagnosis in 38 out of 54 cases (70.37%). A case of hydrocephalus was identified with CT scan and MRI scan, but the final diagnosis of underlying CMV infection could be identified only with serological examination.

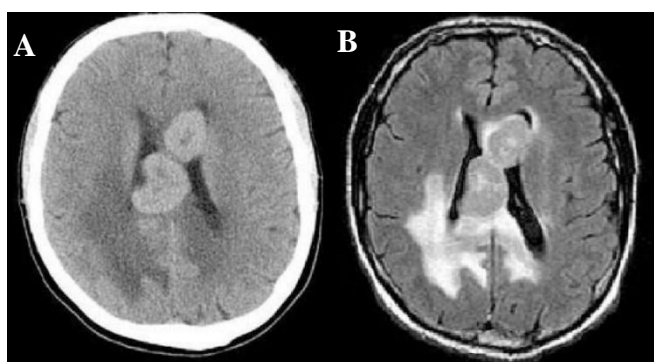
**Figure 1:** Bar chart comparing the number of patients (y axis) having various neurological abnormalities and those detected by CT scan (x axis).



CT scan showed high sensitivity in identifying normal cases, atrophy, CNS lymphoma, infarcts and hydrocephalus, but there were a few false positives

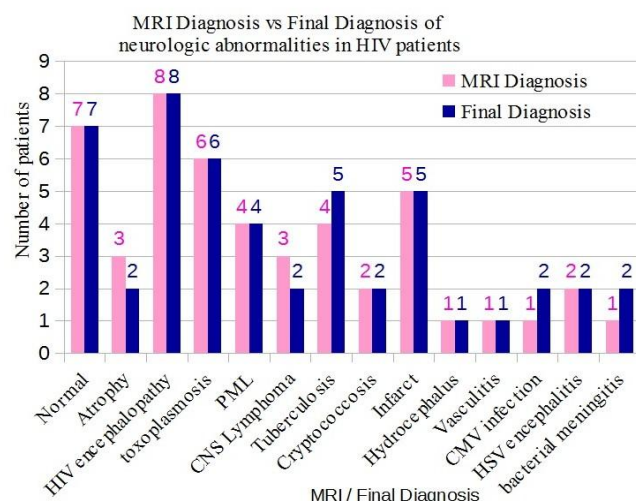
(False positives were noted in 6 out of 8 cases of atrophy in CT scan, 1 out of 5 HIVE, 2 out of 7 toxoplasmosis, 1 out of 3 CNS lymphoma, 2 out of 5 tuberculosis and 3 out of 8 infarcts.) CT scan had poor sensitivity in identifying bacterial meningitis, CMV infection, vasculitis and cryptococcosis [Table 1]. CT scan showed more than 95% specificity in excluding HIVE, toxoplasmosis, PML, CNS lymphoma [figure 2], tuberculosis and hydrocephalus. CT scan showed high positive predictive value in identification of normal cases, PML, hydrocephalus and HSV. More than 90% negative predictive value was noted in all the cases.

of 48 cases (89.58 %). Seven out of 48 patients had normal MRI findings.[figure 3]. The most common abnormality identified in MRI scan were HIVE (16.67%, n=8), toxoplasmosis (12.50 %, n=6), infarcts (10.42%, n=5), PML (8.33%, n=4) and tuberculosis (8.33%, n=4). [Figure 4] MRI scan showed 100 % sensitivity in identifying normal cases, atrophy, HIVE, PML, CNS lymphoma, cryptococcosis, infarcts, hydrocephalus, vasculitis and HSV.[Table 2]. MRI was highly specific. It showed more than 97% specificity for all neurologic lesions. MRI scan showed 100 % positive predictive value in identifying normal cases, HIVE, PML, tuberculosis, cryptococcosis, hydrocephalus, vasculitis, CMV, HSV and bacterial meningitis. The negative predictive value was more than 97% in all the cases.



**Figure 2:** (A) Plain CT scan of brain showing a hyperdense mass lesion in the periventricular location suggesting primary CNS Lymphoma. (B) Pre contrast T2 FLAIR MR image of brain showing this lesion as mildly hyperintense with perilesional white matter oedema.

Among the 48 cases who underwent MRI, 7 patients had normal MRI findings, 3 persons had atrophy only, 8 persons with HIVE, 6 cases with toxoplasmosis, 4 cases of PML, 3 cases of primary CNS lymphoma, 4 persons with tuberculosis, 2 cases of cryptococcosis, 5 cases of infarct, 1 case of vasculopathy with infarct, 1 person with hydrocephalus, 1 case of CMV, 2 cases of HSV encephalitis and 1 case of bacterial meningitis. MRI scan correctly predicted the final diagnosis in 43 out



**Figure 3:** Bar chart comparing the number of patients (y axis) having various neurological abnormalities and those detected by MRI scan (x axis).



**Table 1 :** The prevalence of neurological abnormalities and the sensitivity, specificity, positive predictive value and negative predictive value of CT scan in diagnosis.

	NORMAL		ATROPHY		HIVE		TOXO		PML		CNS LYM		TB		CRYPTO		INFARCT		HYDROC		VASCU		CMV		HSV		BAC MEN	
PREVALANCE	24.07%		3.70%		14.81%		11.11%		7.41%		3.70%		9.26%		3.70%		9.26%		1.86%		1.86%		3.70%		3.70%		3.70%	
	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT
CT POSITIVE	13	0	2	6	4	1	5	2	3	0	2	1	3	2	0	0	5	3	1	0	0	0	0	1	0	0	0	
CT NEGATIVE	0	41	0	46	4	45	1	46	1	50	0	51	2	47	2	52	0	46	0	53	1	53	2	52	1	52	2	52
SENSITIVITY	100		100		50		83.33		75		100		60		0		100		100		0		0		50		0	
SPECIFICITY	100		88.46		97.83		95.83		100		98.08		95.92		100		93.88		100		100		100		100		100	
PPV	100		25		80		71.43		100		66.67		60		NA		62.5		100		NA		NA		100		NA	
NPV	100		100		91.84		97.87		98.04		100		95.92		96.3		100		100		98.15		96.3		98.11		96.3	

HIVE – HIV encephalopathy  
 CNS LYM- CNS Lymphoma  
 VASCU- Vasculitis  
 BACMEN= Bacterial Meningitis  
 TOXO- Toxoplasmosis  
 CRYPTO- Cryptococcosis  
 CMV- Cytomegalovirus  
 PPV- Positive predictive value  
 PML-Progressive multifocal leukoencephalopathy  
 HYDROC- Hydrocephalus  
 HSV- Herpes Simplex Virus  
 NPV- Negative predictive value

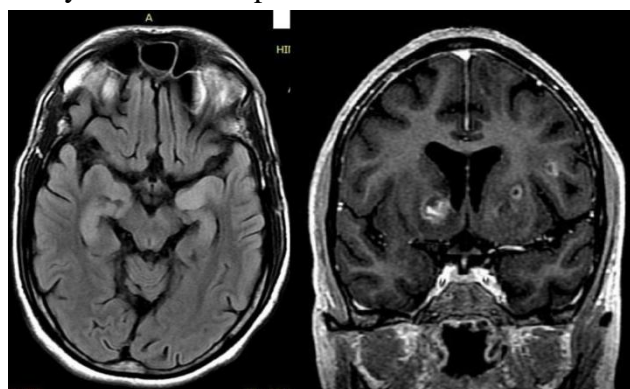
**Table 2 :** The sensitivity, specificity, positive predictive value and negative predictive value of MRI scan in diagnosis of neurological abnormalities.

	NORMAL		ATROPHY		HIVE		TOXO		PML		CNS LYM		TB		CRYPTO		INFARCT		HYDROC		VASCU		CMV		HSV		BAC MEN	
	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT
MRI POSITIVE	7	0	2	1	8	0	5	1	4	0	2	1	4	0	2	0	5	1	1	0	1	0	1	0	2	0	1	0
MRI NEGATIVE	0	41	0	45	0	40	1	41	0	44	0	45	1	43	0	46	0	42	0	47	0	47	1	46	0	46	1	46
SENSITIVITY	100		100		100		83.33		100		100		80		100		100		100		100		50		100		50	
SPECIFICITY	100		97.83		100		97.62		100		97.83		100		100		97.67		100		100		100		100		100	
PPV	100		66.67		100		83.33		100		66.67		100		100		83.33		100		100		100		100		100	
NPV	100		100		100		97.62		100		100		97.73		100		100		100		100		97.87		100		97.87	

HIVE – HIV encephalopathy  
 CNS LYM- CNS Lymphoma  
 VASCU- Vasculitis  
 BACMEN- Bacterial Meningitis  
 TOXO- Toxoplasmosis  
 CRYPTO- Cryptococcosis  
 CMV- Cytomegalovirus  
 PPV- Positive predictive value  
 PML-Progressive multifocal leukoencephalopathy  
 HYDROC- Hydrocephalus  
 HSV- Herpes Simplex Virus  
 NPV- Negative predictive value

**Discussion**

Neurological abnormalities are very common in HIV infected patients despite widespread and early use of antiretroviral and antimicrobial agents [4]. Various studies had been conducted evaluating neurological manifestations in HIV infected patients [5-6]. Neurological abnormalities were present in 75.93% of our patients which were identified using radiological and laboratory data and by treatment response.



**Figure 4:** (A) Pre contrast T2 FLAIR axial MR image of brain showing hyperintense lesions in

bilateral temporal lobes in HSV encephalitis (B). Post contrast coronal FSPGR image of brain showing multiple ring enhancing lesions in bilateral basal ganglia and grey-white matter junction in toxoplasmosis

In our study, maximum number of patients with neurological involvement was in 30 – 39 age group. (38.8 %, n= 21). This is comparable to many previous studies. In Teja VD et al study, most patients showing neurological abnormality were in 30-39 age group with median age of 36 years [7]. In Patel ML et al study [8], 49.5 % patients with neurologic manifestations were in 31-40 year age group with mean of 34.28+/- 7.8 years. In Kausadikar SR et al study, 40% patients were in 31-40 years age group [9]. This age group represents the sexually active age group which may be responsible for the high prevalence. This is of very much importance as it represents a very productive age in the society.

The most common neurological abnormality in patients imaged with CT scan and MRI in our study was HIV encephalopathy (n=8) and the most common opportunistic infections were toxoplasmosis (n=6) and tuberculosis (n=5). In studies by Patel ML et al, Kausadikar SR et al, Rana HM et al <sup>[10]</sup>, Mahajan et al <sup>[11]</sup> and Lanjewar DN et al <sup>[12]</sup>, tuberculosis was the most common cause of opportunistic infections. Normally, when tubercle bacilli reach lung alveoli, alveolar macrophages ingest them. Tubercle bacilli which survive multiply inside macrophages and undergo hematogenous spread to distant sites. Susceptibility to tuberculosis increases in HIV infection due to defective macrophage function <sup>[13]</sup>. Cryptococcal meningitis was more common in Satishchandra P et al study <sup>[14]</sup>. Cryptococcal meningitis usually occurs in patients with very low immune status, resulting in minimal inflammation and frequent absence of clinical signs and symptoms of meningitis and negative CSF examination for cellular response. Hence, in such patients high degree of clinical suspicion is warranted.

In our study MRI was much more sensitive than CT scan in predicting the final diagnosis, CT scan showing a sensitivity of 70.37 % while MRI showing a sensitivity of 89.58%. This high sensitivity of MRI when compared to CT scan was also noted in previous study by Wilson AJ et al <sup>[15]</sup> where neurological abnormalities were detected in 74% of HIV infected patients with neurological presentations while CT scan identified them only in 32%. In our study CT was unable to identify cryptococcosis, CMV infection, bacterial meningitis and vasculitis which were all identified in MRI except for one patient each with bacterial meningitis and vasculitis. This could be attributed to the excellent soft tissue resolution of MRI and also due to the availability of multiple sequences in MRI which makes identification and characterisation of intracranial lesions easy <sup>[16]</sup>.

There were a few limitations in this study. The study was conducted in only a small number of patients (n =54) as the duration of study was only

1.5 years. Also, all HIV patients with neurologic symptoms requested for CT scan or MRI might not have reached Radiodiagnosis department, which could alter the prevalence of various neurological abnormalities. The diagnostic accuracy of the tests might also be low if the prevalence of the neurological abnormalities is low in the pool of HIV patients which was also not taken into consideration in this study. Final diagnosis was made considering many factors including favourable response to treatment; however, clinical course could also be unrelated to treatment. Lack of autopsies which could substantiate a clinical diagnosis was also a limitation.

### Conclusion

When compared to CT scan, MRI is much more sensitive in identification of various neurological abnormalities in HIV infected patients. HIV encephalopathy, infarcts and opportunistic infections like tuberculosis and toxoplasmosis are common abnormalities identified in these patients. A strong clinical suspicion leads to prompt diagnosis resulting in early treatment which can improve the quality of life and reduce the mortality.

**Conflict of Interest:** No conflict of interest

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