A STUDY ON NEUROLOGICAL MANIFESTATIONS IN HIV PATIENTS

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In partial fulfillment
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BRANCH – I

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CERTIFICATE

This is to certify that the dissertation entitled **"Study on Neurological Manifestations in HIV patients"**is a bonafide work done by **Dr. P.MONNA MOHAMED JABER** in **M.D BRANCH I GENERAL MEDICINE** at Government Coimbatore Medical College, Coimbatore, to be submitted to The Tamil Nadu Dr.M.G.R Medical University, in fulfillment of the University Rules and Regulation for the award of M.D. Degree Branch I General Medicine, under my supervision and guidance, during the academic year 2009-2012.

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DECLARATION

I solemnly declare that this dissertation **"A Study on Neurological Manifestations in HIV patients"** was prepared by me at Govt. Coimbatore Medical College hospital, Coimbatore., under the guidance and supervision of **Prof. Dr.S.VEERAKESARI, M.D.,** HOD of General Medicine, Govt. Coimbatore Medical College hospital, Coimbatore.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in fulfillment of the University regulations for the award of the degree of M.D. Branch I General Medicine.

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ACRONYMS

AIDS	- Acquired Immuno Deficiency Syndrome
ADC	- AIDS Dementia Complex
AIDP	- Acute inflammatory demyelinating polyneuropathy
ALC	-Absolute Lymphocyte Count
ANOVA	-Analysis of variance
ART	- Anti Retroviral Treatment
BBB	- Blood Brain Barrier
CCR	- Chemokine Receptor
CDC	- Center For Disease Control
CD4	- Cluster of Differention 4
CM	- Cryptococcal Meningitis
CMV	- Cytomegalovirus
CNS	- Central Nervous System
CSF	- Cerebrospinal Fluid
CSW	- Commercial Sex Worker
CK	- Creatine Kinase
CVS	- Cardiovascular System
CVA	- Cerebrovascular Accident
DNA	- Deoxy Ribo Neuclic Acid
DSP	- Distal Symmetric Polyneuropathy
ELISA	- Enzyme Linked Immunosorbent Assay
EMG	- Electromyography
ESR	- Erythrocyte Sedimentation Rate
FND	- Focal Neurological Deficit
HAN	- HIV Associated Neurocognitive Disorders

HAART	- Highly Active Antiretroviral Treatment
HBV	- Hepatitis B Virus
HIV	- Human Immunodeficiency Virus
HCV	- Hepatitis C Virus
HMF	- Higher Mental Function
HTLV	- Human T Cell Lymphoma Virus
HZ	- Herpes Zoster
ICAM	-intercellular adhesion molecule
IDP	- Inflammatory Demyelinating Poly Neuropathy
IFN	- γ - Interferon -Gama
IgM	- Immunoglobulin M
INH	- Isoniazid
IL-1	- Interleukin-1
IL-6	- Interleukin-6
MCH	- Major Histocompatability Complex
MMSE	-Mini Mental Score Examination
NAA	- n-acetylaspartate
MRI	- Magnetic Resonance Imaging
NACO	- National Aids Control Organisation
NMDA	- N-Methyl D-Aspartate
PCP	- Pneumocystis Carinii Pneumonia
PCR	- Polymerase Chain Reaction
PCNSL	- Primary Central Nervous System Lymphoma
PML	- Progressive Multifocal Leukoencephalopathy
RNA	- Ribo Nucleic Acid
STD	- Sexually Transmitted Disease
TB	- Tuberculosis
TBM	- Tuberculous meningitis

TE	- Toxoplasma Encephalitis
TGF	- β-Tissue Growth Factor-Beta
TLC	- Total Leukocyte Count
TNF	- Tumour Necrosis Factor-Alpha
TM	- Transverse Myelitis
VCAM	-vascular cell adhesion molecule
VDRL	- Venereal Disease Research Laboratory
VIP	- Vasoactive Intestinal Polypeptide
WHO	- World Health Organization
ZDV	- Zidovudine

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INTRODUCTION

On the cusp of fourth decade of the AIDS epidemic, HIV (Human Immunodeficiency Virus) is still one of the leading infectious killer claiming more than 25 million lives over the last 30 yrs. In 2010 there was approximately 34 million people living with HIV ,more than 2/3rd living in sub Saharan Africa and southeast Asia[1].

HIV/AIDS causes a wide spectrum of disease manifestations. The nervous system is among the most frequent and serious targets of HIV infection. 40% to 70% of all persons infected with HIV develop symptomatic neurological disorders.Allthough nervous system involvement typically occurs with profound immunosuppression and in the presence of other acquired immunodeficiency syndrome (AIDS) defining illnesses, yet in 10% to 20% of HIV seropositive persons it heralds AIDS[2].All levels of neuraxis can be involve including the brain, meninges, spinal cord, peripheral nerve and muscle.CNS infections are the third commonest cause of morbidity and second commonest cause of mortality in HIV patients. Neurological illness may occur throughout the course of infection from seroconversion to full blown AIDS.

The neurological problems fall in to four major catogaries ;1.neurological disease caused by HIV itself, 2. HIV related neoplasms, 3.oppurtunistic infection of the nervous system, 4.adverse effects of medical therapy.

With the advent of antiretroviral drugs and effective chemoprophylaxis for OIs, the life span for patients infected with HIV has increased considerably. In a resource-limited country such as India, where antiretroviral drugs are not yet affordable for large sections of the population, cheap and effective chemoprophylaxis for OIs has significantly reduced morbidity and increased longevity. All this has resulted in the observance of a large number of clinical neurologic manifestations

The pattern in India appears to differ from the classical literature in that Neurotuberculosis leads the list of opportunistic infections and regional variability has been reported within India[3,4]. A study of the various neurologic manifestations that can be seen due to HIV infection and their association with the severity of immunodeficiency as judged by the CD4+ cell count is presented here.

AIM OF THE STUDY

1) To document neurologic events in HIV cases and to determine the Prevalence of HIV-related neurological disorders in CMCH.

2) To study the diverse clinical presentations of neurologic abnormalities, and to correlate these with the CD4 count.

3) To compare the differences in the Neurological manifestations of HIV infection in patients in this study with the various studies carried out in western countries and in north India.

REVIEW OF LITERATURE

Clinically apparent and frequently debilitating neurologic disease is common with HIV infection. Approximately one half of all HIV-infected patients will develop clinically significant neurologic disease, and the frequency with which neuropathologic abnormalities are detected at autopsy in some series exceeds 75%, suggesting that neurologic findings are often overlooked[5,6]. Not surprisingly, careful neurologic examination, even in the absence of specific complaints by the HIV-infected patient, often reveals evidence of central or peripheral nervous system dysfunction. Although neurologic disease typically occurs with advanced disease and profound immunosuppression, it may also occur during early stages of the infection. In as many as 20% of individuals, neurologic disease is the harbinger of AIDS[5]. The spectrum of neurologic disorders that complicate HIV infection is extremely broad; any part of the neuraxis may be affected. Additionally, the complexity of evaluating the HIV-infected person with neurologic disease is increased by the relatively high frequency with which more than one disease concurrently affects the nervous system.

HIV-associated neurologic syndromes can be classified into primary HIV neurologic disease (in which HIV is both necessary and sufficient to cause the illness), secondary or opportunistic neurologic disease (in which HIV interacts with other pathogens, resulting in opportunistic infections and tumors), and treatment-related neurologic disease.

NEUROPATHOGENESIS

Development of primary HIV neurological disease depends on a number of factors such as degree of immunosuppressant and the molecular biology of the viral strain, particularly its neurovirulence.

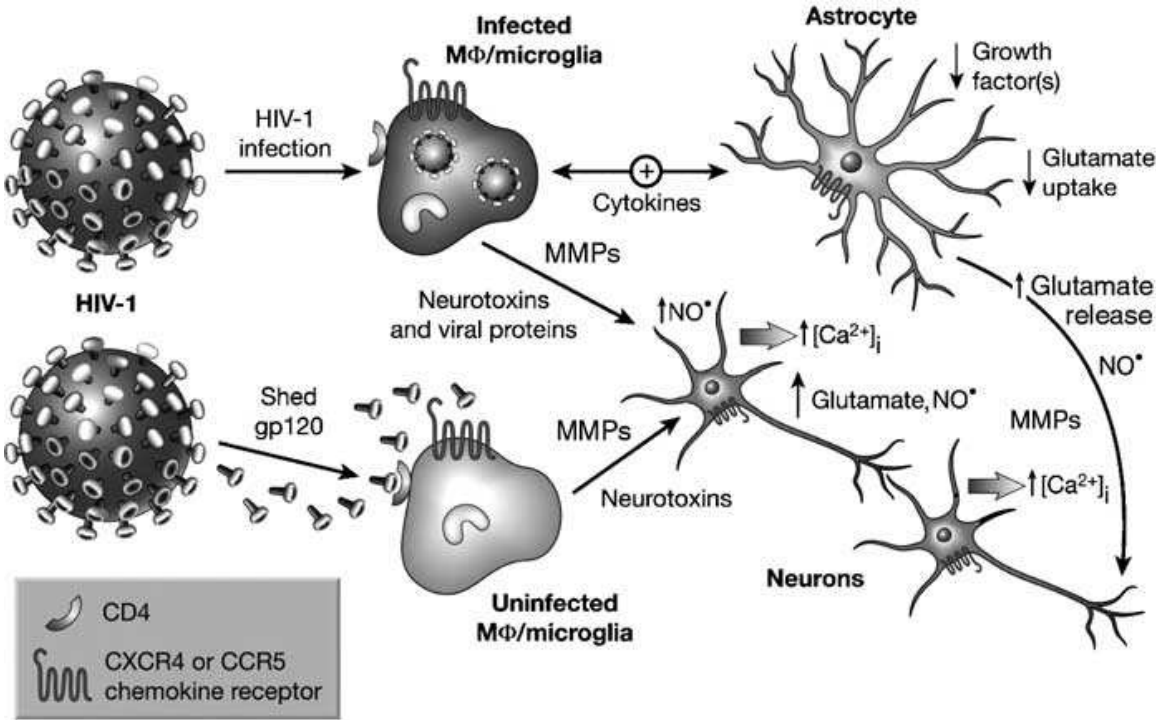
HIV quickly enters the brain after initial exposure, probably through infected monocytes and lymphocytes that cross the blood brain barrier (BBB)[7].

HIV entry into brain is felt to be due, at least in part, to the ability of virus infected and immune-activated macrophages to induce adhesion molecules such as E selectin and vascular cell adhesion molecule-1 (VCAM-1) on brain endothelium.Other studies have demonstrated that HIV gp120 enhances the expression of intercellular adhesion molecule-1 (ICAM-1) in glial cells; this effect may facilitate entry of HIV-infected cells into the CNS and may promote syncytia formation.

The HIV-mediated effects on brain tissue are due to a combination of direct effects, either toxic or function-inhibitory of gp120 on neuronal cells and effects of a variety of neurotoxins released from infiltrating monocytes, resident microglial cells, and astrocytes. In this regard, it has been demonstrated that both HIV-1 Nef and Tat can induce chemotaxis of leukocytes, including monocytes, into the CNS. Neurotoxins can be released from monocytes as a consequence of infection and/or immune activation. Monocyte-derived neurotoxic factors have been reported to kill neurons via the N-methyl-D-aspartate (NMDA) receptor. In addition, HIV gp120 shed by virus-infected monocytes could cause neurotoxicity by antagonizing the function of vasoactive intestinal peptide (VIP), by elevating intracellular calcium levels, and by decreasing nerve growth factor levels in the cerebral cortex.

The likelihood that HIV or its products are involved in neuropathogenesis is supported by the observation that neuropsychiatric abnormalities may undergo remarkable and rapid improvement upon the initiation of antiretroviral therapy, particularly in HIV-infected children[8]

Fig 1: Current model of neuronal injury induced by HIV-1 Infection[9].



One model of HIV encephalitis identified a pattern of monocytes trafficking from bone marrow as a correlate to encephalitis with newly arriving brain macrophages demonstrating recent transmigration[10]. The demonstration was most consistent with bone marrow and circulating monocytes a finding that peripheral monocytes HIV DNA levels correlate to HIV-associated

neurocognitive disorders HAND[11].Together, these data raise concern that peripheral reservoirs continue to play an active role in brain injury.

PRIMARY HIV-ASSOCIATED DISORDERS OF THE NERVOUS SYSTEM

Aseptic meningitis

A minority of seroconverters in acute HIV infection will experience a neurologic event that brings them to medical attention, such as aseptic meningitis, Bell's palsy[12] or inflammatory neuropathy. Neurological symptoms may occur before an HIV diagnosis is suspected, e.g., before there are sufficient HIV antibodies to produce a positive HIV enzyme-linked immunosorbent antibody(ELISA, also called an HIV enzyme immunoassay). In such cases, a Western Blot or a polymerase chain reaction (PCR) test for HIV may lead to the diagnosis. Early diagnosis of acute HIV infection is important, as these individuals are at high risk to transmit the virus.

The most common neurological syndrome associated with primary HIV infection is an acute aseptic (viral) meningitis or meningoencephalitis. The symptoms are similar to other viral meningitides, with fever, headache, stiff neck, and photophobia. Cerebrospinal fluid (CSF) shows a mild lymphocytic

pleocytosis, normal or slightly elevated total protein, and normal glucose . HIV may be detectable by antigen or PCR testing[13]. This syndrome, which cannot be clinically differentiated from other viral meningitis, usually resolves spontaneously within 2 to 4 weeks, however, in some patients it may become chronic[14].

HIV Associated Neurocognitive Disorders (HAND)

One of the most frequent and enigmatic of the neurological complications of HIV infection is a chronic neurodegenerative condition characterized by cognitive, central motor and behavioral abnormalities. A variety of names (e.g. AIDS Dementia Complex, HIV Associated Dementia, HIV Associated Cognitive Motor Complex) have been applied to this syndrome. Recently, HIV Associated Neurocognitive Disorder (HAND)[15] has become a widely accepted nosology for classifying individuals with varying levels of HIV-associated neurocognitive deficits. HAND is stratified into

1) asymptomatic neurocognitive impairment (ANI)

2) minor neurocognitive disorder (MND) and

3) HIV Associated Dementia (HAD).

ANI is characterized by a subclinical decline in cognition. MND is characterized as mild decline in cognition in addition to mild everyday functioning impairment that affects the more difficult activities of daily living). HAD is characterized by significant decline in cognition along with a significant degree of functional impairment that affects routine activities[16].

There is no diagnostic marker or combination of markers for HAND. The diagnosis is made in HIV+ patients with cognitive impairment, after ruling out confounding conditions (CNS OI, neurosyphilis, substance abuse, delirium, toxic-metabolic disorders, psychiatric disease, and age related dementias).

HAND has been characterized as a "subcortical dementia"[17], in which deficits in working memory (e.g., "short-term" memory, the ability to remember information over a brief period of time) and executive function (e.g., planning, cognitive flexibility, abstract thinking, rule acquisition, initiating appropriate actions and inhibiting inappropriate actions) tend to occur early on. Deficits in delayed recall are more typical of "cortical" dementias such as Alzheimer's disease.

HIV can have profound effects on the pyramidal and extrapyramidal motor systems. Milder manifestations of CNS motor impairment include ataxia, motor slowing, incoordination, and tremor. This may progress to disabling weakness, spasticity, extrapyramidal movement disorders, and paraparesis[18].

Behavioral effects of HAND include apathy, irritability, and psychomotor retardation[19], which can be mistaken for depression. Sidtis and Price[20] developed a staging system for AIDS dementia complex that classifies patients from normal (grade 0) to end-stage vegetative state (grade 4). Grade 0.5 (subclinical dementia) comprises patients whose disease may be difficult to diagnose. The diagnosis of dementia accomplished by Mini Mental Score Examination (MMSE). It is advisable for all patients with a diagnosis of HIV infection to have baseline MMSE. Historically, the onset of HAND was associated with low CD4+ counts, other AIDS symptoms, elevated CSF viral load, and elevated CSF markers of immune activation[21](e.g. beta 2 microglobulin and neopterin) .

The traditional neuroimaging approach is useful in excluding structural or inflammatory processes, such as abscess, or tumor, that may mimic HAND,

but is limited as a diagnostic marker. The HAND brain may appear grossly normal until advanced disease, when atrophy may be noted. White matter changes may appear, typically in the periventricular region.

Lentz et al[22], reported on subjects followed from early seroconversion and reported initial decline in n-acetylaspartate (NAA), a marker of neuronal viability, in the frontocortical gray matter.

Neurological and neuropsychological improvement of HAND after treatment with antiretrovirals was established with studies of zidovudine monotherapy in randomized placebo-controlled trials[23]. Schmitt and associates[24] reported that AIDS patients receiving ZDV 1000 mg/day had improved neuropsychological performance compared with patients receiving placebo. Several experimental agents are under investigation in the treatment of HIV dementia, including nimodipine (calcium-channel blocker), memantine (NMDA antagonist),delavirdine (non nucleoside reverse transcriptase inhibitor), and peptide T(pentapeptide analogue of gpl20) [25].

Myelopathy

Vacuolar myelopathy is the most common spinal cord disease in AIDS, found in up to 30% of Autopsies in the pre-cART era . It is under diagnosed[26] and must be differentiated from other causes of myelopathy such as infection with Human T-cell lymphotropic virus (HTLV) I or II; herpes simplex 1 or 2, varicella zoster, cytomegalovirus, enteroviruses, syphilis and tuberculosis, tumors, and nutritional deficiencies such as B12[27].

The clinical presentation of HIV VM is slowly progressive leg weakness, which may be asymmetric at first, spasticity, dorsal column (vibration, position) sensory loss, ataxic gait, and urinary frequency and urgency[28]. Erectile dysfunction is an early sign in men. The diagnosis should be questioned if symptoms present in an acute fashion, the arms are affected, there is a sensory level, or if there is back pain.

The most important test is a spinal MRI, to rule out abscess or tumor. In many HIV VM cases, the MRI is normal. Some will have high signal hyperintense areas on T2 weighted imaging, primarily in the thoracic region and affecting the posterior columns, that do not enhance with contrast; these areas correlate to vacuolation on histopathology[29]. A lumbar puncture is important to exclude treatable infections or carcinomatous meningitis.

The precise pathophysiology of HIV VM is unknown. The distribution of pathology, involving the posterior columns and pyramidal tracts, resembles B12 deficiency[30]. Suspected mechanisms include defective methylation due to a deficiency of S-adenosylmethionine , triggered by inflammatory products secreted by activated macrophages and microglia[31].

There is no specific treatment for HIV VM. A pilot, open label study of L-methionine to address the suspected abnormality of transmethylation mechanisms in HIV VM did not show benefit[32]. There are case reports of improvement with cART.Patients with HIV VM benefit from physical and occupational therapy, baclofen, tizanidine, dantrolene, and intramuscular botulinum toxin to manage spasticity, pain management, and anticholinergic drugs to improve bladder function[18].

HIV associated Peripheral Neuropathies

Many peripheral neuropathic syndromes have been reported in the context of HIV infection. The significant types are ;

- HIV-associated distal sensory neuropathy
- Neurotoxic nucleoside neuropathy
- Inflammatory demyelinating neuropathy

- Progressive Polyradiculopathy
- Mononueritis multiplex.

HIV associated distal peripheral sensory neuropathy (DSPN)

HIV associated DSPN(also called predominantly sensory neuropathy, or distal symmetrical peripheral neuropathy), is the most common neurological problem in AIDS[33], with incidences ranging from 19-66%, depending upon the age, disease stage, and treatment history of the cohort[34]. The risk factors for HIV DSPN are older age, history of alcohol abuse, and advanced HIV disease (e.g., a low nadir CD4+ count and high plasma HIV viral load)[35], prior use of a neurotoxic antiretroviral drug (e.g., didanosine, stavudine, zalcitabine), and diabetes.

The most universally reported symptoms are paresthesias[36], that virtually always begin in the feet, as this is a length-dependent neuropathy. Patients complain of burning, of numbness, of hot or cold sensations, and of episodic electric-shock like sensations. Most patients do not develop any motor weakness or muscle wasting until late in their course, and this is limited to the distal extremities[37.]The most common physical findings are decreased or absent ankle jerks, diminished vibratory sensation in the legs, and increased

threshold to temperature and pinprick (alternatively, some patients develop hyperesthesia)[38].

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The pathogenesis of HIV DSPN is unknown. The HIV protein gp120 is also neurotoxic, causing hyperesthesia, allodynia, and spinal gliosis[39]. In most cases, an electromyogram (EMG) and nerve conduction studies (NCS) are not necessary to diagnose HIV DSPN[40]. It is important to search for processes that can mimic or exacerbate HIV DSPN, including syphilis, diabetes, B12 or folate deficiency, thyroid disease, hepatitis C virus, and any neurotoxic medication.

Symptomatic therapy for DSPN includes analgesics, tricyclic antidepressants, anticonvulsants, and topical capsaicin. Amitriptyline, mexiletine, nerve growth factor, and acupuncture are being evaluated in controlled clinical trials of painful HIV neuropathy. Lamotrigine[41], high-concentration capsaicin dermal patch[42], cannabinoids and gabapentin showed positive results.

Nucleoside neuropathy in HIV patients

Nucleoside neuropathy also called antiretroviral toxic neuropathy, neurotoxic neuropathy, has classically been associated with three NRTI drugs: didanosine (ddI), zalcitabine (ddC), and stavudine (d4T). Other risk factors include another, prior neuropathy, diabetes, alcoholism, poor nutrition, using higher doses of the offending nucleoside, and use of more than one nucleoside[27]. The clinical and electrophysiological features of neurotoxic neuropathy are very similar to HIV DSPN[43], but usually begin within six months of starting the offending drug, with a peak around 3 months[44]. It has been proposed that mitochondrial toxicity[45], and specific host genetic polymorphisms[46] may predispose to nucleoside neuropathy. The only specific treatment is to remove the offending drug; if this is impossible, it should be maintained at the lowest dose.

Inflammatory Demyelinating Polyneuropathies (IDP)

The true prevalence of this complication is unknown, but it appears to be relatively rare. There are two major types of HIV inflammatory demyelinating polyneuropathies (HIV IDP). Acute IDP is similar to Guillain- Barre syndrome, and often occurs during or near primary

infection[47]. Patients develop the rapid onset of ascending weakness, areflexia, autonomic instability, and some (usually minor) sensory symptoms[48], but bowel and bladder function is spared. The disease can progress to involve the muscles of respiration. Unlike non-HIV Guillain Barre, there is usually a mild lymphocytic pleocytosis. Electrophysiological studies show patchy distribution of abnormalities, including slow or absent nerve conduction, and abnormal F-waves[49]. Treatment consists of supportive care, intravenous gamma globulin, plasma exchange, and possibly cART[50] .

A chronic IDP (CIDP) may occur in late infection and is often associated with a CD4+ count of under 50 cells/mm^3 [51]. Unlike acute HIV IDP, this syndrome progresses slowly and may have a relapsing and remitting nature. It must be differentiated from neuropathies caused by CMV and related viruses. Treatment of HIV CIDP is similar to that of non-HIV related CIDP, with the exception for the need to control HIV infection.

Mononeuropathy Multiplex

Patients with mononeuropathy multiplex develop multifocal, asymmetric, cranial or peripheral nerve lesions, including facial or laryngeal palsy, wristdrop or footdrop, and other neuropathic symptoms. In the early stages

of HIV infection, mononeuropathy multiplex is usually limited to one or few nerves and resolves spontaneously without treatment. In advanced HIV disease, particularly when CD4 counts fall below 50 cells/cumm, this neuropathy may progress rapidly to quadriparesis. When the neurologic deficits are diffuse and confluent, mononeuropathy multiplex may be mistaken for IDP, DSP, or progressive polyradiculopathy. Said and colleagues[52] .have reported that the extensive form of mononeuropathy multiplex results from primary CMV infection and that these patients improve with ganciclovir therapy.

Progressive Polyradiculopathy (PP)

The presenting symptoms of progressive polyradiculopathy are rapidly progressive lower extremity and sacral paresthesias, flaccid paraparesis, areflexia, sensory loss, and urinary retention. Cerebrospinal fluid examination reveals a marked pleocytosis, containing hundreds to thousands of polymorphonuclear leukocytes. Although cerebrospinal fluid culture is positive in only approximately 50% of these patients, there is considerable clinical and pathologic evidence that most cases of AIDS-associated progressive polyradiculopathy result from primary CMV infection of nerve roots[53].

Approximately 50% of patients with progressive polyradiculopathy have neurologic improvement or stabilization after therapy with ganciclovir[54] or foscarnet. Less common causes of AIDS-associated progressive polyradiculopathy are neurosyphilis, leptomeningeal lymphoma, and tuberculosis[47].

Myopathy

HIV-associated myopathy may occur at all stages of HIV infection[55]. Proximal muscle weakness is the predominant presenting symptom. Myalgia is present in 25% to 50% of affected patients. Weight loss commonly accompanies myopathy, and in some patients, myopathy is the underlying cause of HIV wasting syndrome.The most sensitive serologic test for HIV myopathy, as in other primary muscle diseases, is creatine kinase (CK). Simpson and coworkers reported that CK is elevated in 92% of patients with myopathy, with a median of 478 U/L. Electromyography (EMG) is a sensitive diagnostic test in HIV myopathy and is particularly helpful in challenging cases[56].

The most common finding on muscle biopsy in HIV-associated myopathy is

scattered myofiber degeneration, with occasional associated inflammatory infiltrates.Other pathologic findings in HIV myopathy include myofiber inclusions, such as nemaline rod bodies, cytoplasmic bodies, and various mitochondrial abnormalities.

The pathogenesis of HIV-associated myopathy is unknown, although immune mechanisms are likely as in HIV-negative polymyositis. Rarely, other opportunistic organisms may infect muscle of patients with AIDS, including Toxoplasma gondii, CMV, Microsporida, Cryptococcus neoformans, Mycobacterium avium-intracellulare and Staphylococcus aureus.

ZDV has been implicated as a cause of myopathy by numerous authors[57]. The degree to which ZDV toxicity contributes to underlying HIV-associated myopathy and whether there are distinguishing features between these disorders have been the subject of debate.

Because it may be difficult to identify prospectively patients with ZDV myotoxicity, the initial management of patients with significant limb weakness and objective evidence of myopathy includes ZDV dose reduction or withdrawal[58.] Simpson DM et al showed only a few patients with myopathy improves with ZDV withdrawal, suggesting that in most subjects

HIV rather than ZDV causes myopathy[45]. In several retrospective series, prednisone therapy improved strength in most patients with HIV-associated myopathy, with tolerable adverse effects. Patients with or without inflammatory infiltrates in muscle may respond to steroid therapy[59].

SECONDARY HIV-ASSOCIATED DISORDERS OF THE NERVOUS SYSTEM

INTRACRANIAL OPPORTUNISTIC INFECTIONS

Neurotuberculosis

Disease caused by *Mycobacterium tuberculosis* is one of the most important opportunistic infectious diseases in acquired immunodeficiency syndrome (AIDS) patients.In HIV-infected Patients.neurotuberculosis usually appears in the context of disseminated tuberculosis and is probably the result of hematogenous spread.

CNS involvement: M. Tuberculosis can cause meningitis, tuberculoma, brain abscess, myelopathy, or radiculopathy. It can occur at any stage of HIV infection, and is often intracerebral and accompanied by anergy to skin testing. Patients present with insidious onset of headache, fever and malaise, followed by meningismus, cranial nerve deficits, seizures and altered mental status. The symptomatology of patients with focal tuberculous lesions in the

brain and meningitis is usually indistinguishable from that presented by patients with TM alone[60]. In patients in whom the diagnosis is made based on the presence of a cerebral mass alone, focal neurologic signs and seizures predominate. However, even in patients with focal cerebral lesions caused by tuberculosis, analysis of CSF will often also provide evidence for the presence of TM. In addition, patients with focal cerebral tuberculous lesions will often have concomitant tuberculosis infection outside of the central nervous system[61].

Stroke may occur when M.tuberculosis infects the intracranial arteries, most commonly in the anterior circulation. A patient with AIDS who have a focal CNS lesion without focal neurological signs are more likely to have Toxoplasmosis than Tubeculosis[62]. In patients with Mycobacterium avium intracellulare, single or multiple mass lesions are more common than meningitis.

Computed tomographic characteristics are diverse and include ring-enhancing lesions and hypodense areas. On rare occasion, the CSF may be normal. Negative microbiologic studies of the CSF are not unusual, resulting in treatment for presumptive infection. Meningeal or brain biopsy may be

required to firmly establish the diagnosis. The response of AIDS patients to the standard therapy for M.tuberculosis is generally gratifying.

Toxoplasmosis encephalitis (TE)

Toxoplasma gondii is a ubiquitous intracellular protozoan pathogen of both humans and animals. The definitive host is the cat, but the parasite can be carried by all mammals. Infection can be acquired transplacentally, or by ingesting contaminated water, undercooked meat, soil, or cat feces. The parasite may remain latent for years; cases of AIDS-associated T*oxoplasmosis* encephalitis (TE) almost always result from reactivation, usually when the CD4+ count has declined below 200 cells/mm^3; higher risk is present when the CD4+ is under 50 cells/mm^3 [63].

Fever, headache, focal neurological deficit, cognitive dysfunction, seizures, and altered mental status are the most common presenting symptoms of TE[64]. Because these are highly inflammatory and necrotic lesions with mass effect, elevated intracranial pressure is often a serious problem.

The typical neuroimaging presentation includes multiple (in seventy percent of cases), contrast-enhancing lesions, frequently surrounded by edema[65].

Most lesions are supratentorial, and located at the gray-white matter junction or in the basal ganglia. MRI typically shows several T2 weighted hyperintense lesions with enhancement on postcontrast T1 images[65]. The most important differential diagnosis in AIDS patients is primary central nervous system lymphoma (PCNSL). Some investigators advocate the use of thallium-201 brain single-photon emission CT[66] or positron emission tomography (PET) to differentiate between PCNSL (which has a high rate of uptake) and TE (which does not). However, most physicians still require a tissue diagnosis before treating a patient for PCNSL because of the lack of specificity of these techniques. Cerebrospinal fluid (CSF) frequently is not sampled in TE, because the mass lesions may make lumbar puncture unsafe. It is useful in excluding other pathogens. Almost all AIDS patients with TE are have toxoplasma immunoglobulin G (IgG) antibodies in blood. While a definitive diagnosis requires brain biopsy, a response to empiric toxoplasmosis treatment is also considered to be diagnostic ; failure to respond is an indication for biopsy[63].

The treatment of choice for toxoplasmosis encephalitis is a combination of pyrimethamine (200 mg oral loading dose followed by 50 mg by mouth per day, plus sulfadiazine 1 gram by mouth, four times a day (to treat the

parasite) and leucovorin (folinic acid) 10 mg by mouth per day, to reduce toxicity caused by pyrimethamine[63]. An alternative regimen is pyrimethamine 200 mg by mouth loading dose followed by 50 mg by mouth per day, plus clindamycin 600 mg by mouth four times a day plus leucovorin 10 mg per day. Acute therapy should be continued for at least six weeks, provided that the patient is improving, and longer in cases with extensive disease.

Cryptococal meningitis (CM)

Cryptococcus neoformans is an encapsulated yeast ,is the most common central nervous system fungal infection in HIV-infected patients .

In AIDS, the most common presentation is a subacute meningoencephalitis, usually in a patient with under 100 CD4+ cells/mm^3. Common presenting symptoms of CM include malaise, headache, and fever. As the disease progresses, patients may develop seizures and signs of increased intracranial pressure (nausea, vomiting, visual loss, diplopia, coma). Cryptococcus may cause minimal inflammation in AIDS patients with impaired immune defenses. This may explain why classic symptoms and signs of meningitis,such as neck stiffness and photophobia, are often absent.

A diagnosis of CM can be made by visualizing the yeast in CSF, using India ink; or by detecting cryptococcal antigen in the CSF using the latex agglutination test . If lumbar puncture is contraindicated, a presumptive diagnosis can be made with a serum antigen test. AIDS patients may not have a CSF cellular pleocytosis, abnormal protein, or low CSF glucose. Neuroimaging may be normal, but abnormalities such as masses (cryptococcomas), dilated perivascular spaces, or pseudocysts, are associated with higher blood and CSF antigen titers[68].

Immediate treatment is essential to prevent loss of brain and loss of life, as this is a lethal disease and even with optimal treatment, the mortality rate is still 15%[69]. The recommended initial standard treatment is amphotericin B, at a dose of 0.7 mg/kg daily, combined with flucytosine, at a dose of 100 mg/kg daily in four divided doses, for at least 2 weeks for those with normal renal function[63].

Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the CNS. It is caused by the *John Cunningham virus* (JCV), a polyoma virus found world-wide, with a seroprevalence of 70-90%[70]. Most

cases of AIDS PML occur during severe immunosuppression (under 100 CD4+cells/mm^3) although exceptions occur in about 11% of cases[71]. Most present with the subacute onset of altered mental status, accompanied by focal symptoms referable to the location of the one or more PML lesions, such as hemiparesis, hemianopsia, ataxia, vertigo, speech disorders, and seizures[72].

A definitive diagnosis is established by biopsy or autopsy. However, a diagnosis of probable PML can be made with a supportive clinical history along with correlative radiological and laboratory findings. The most common neuroimaging findings[73] are one or more space-occupying white matter lesions that are non-enhancing, hyperintense on T2 and hypointense on T1, and spare the cortical U-fibers. Cerebrospinal fluid examination (CSF) is invaluable in ruling out other infections, but otherwise is nonspecific, with mild pleocytosis, elevated total protein, and normal glucose. A positive JCV PCR is considered diagnostic in a case with typical clinical and imaging features.

Neuropathologic findings are characterized by multiple areas of pronounced white matter demyelination, with frequent involvement of the gray-white matter junction and cortical gray matter in the most severe cases. The typical

histological features of PML are a triad consisting of large ballooned oligodendroglial cells, with nuclear inclusions containing large numbers of virions; enlarged, bizarre astrocytes; and foci of demyelination.

There is no specific treatment for PML with or without AIDS. Multiple agents have been tried without success including topotecan[74], cytarabine[75], and cidofovir . However, cART has improved the course of AIDS PML, decreasing the mortality rate, improving the neuroimaging features, improving survival, and decreasing CSF JCV viral load[72].

Cytomegalovirus

Cytomegalovirus (CMV), a member of the Herpesvirus family, can infect the brain, spinal cord, meninges, retina, the dorsal root ganglion of peripheral nerves, and many visceral organs[76]. CMV encephalitis has been diagnosed at autopsy in 6% to 40% of AIDS patients with dementia[77] . Typically, CMV of the nervous system presents in individuals with CD4+ counts under 50 CD4+ cells/mm^3. Neurological CMV disease can present as encephalitis, ventriculitis, myelitis, radiculoganglionitis and peripheral polyneuropathy, or various combinations thereof[78].

Presenting signs and symptoms are extremely variable depending upon the area affected; CMV encephalitis and ventriculitis may present with fever, lethargy, confusion, or coma, seizures, and cranial nerve palsies, ataxia and hemiparesis, or even coma. CMV infection of the spinal cord may cause either a transverse myelitis or a myeloradiculitis characterized by flaccid paraparesis associated with back pain, incontinence, areflexia, paresthesias and sensory loss, and ascending weakness[79].

The CSF CMV PCR is considered the gold standard for identifying and quantifying CNS CMV and for following the response to therapy[80].

The recommended treatment is intravenous ganciclovir, at an induction dose of 5mg/kg twice daily. Intravenous foscarnet 90 mg/kg twice a day, can be used in lieu of ganciclovir but has greater renal toxicity.

HIV ASSOCIATED NEOPLASMS

Primary CNS LYMPHOMA (PCNSL) in AIDS

Primary CNS lymphoma (PCNSL) arises in and is confined to, the CNS. It is second most common mass lesion in AIDS. The major risk factor is a CD4+ count under 100 cells/mm^3. In the setting of immunosuppression, PCNSL is almost always associated with Epstein-Barr Virus (EBV)[81], a

ubiquitous herpes virus with a seroprevalence of 90%. In AIDS, immune surveillance fails and the immortalized EBV-infected B cells are no longer held in check[82]. Thus the risk of PCNSL is greatly increased.

The presenting symptoms of PCNSL include lethargy, confusion, impaired memory, headache, seizures, or focal weakness. Many patients develop cranial neuropathies and/or ocular involvement. Increased intracranial pressure and herniation can result in papilledema, and coma if untreated.

The usual neuroimaging findings on CT or MRI are one or sometimes multiple, contrast-enhancing lesions surrounded by edema, with mass effect. On MRI, they are hyperintense on T1 imaging and often show a periventricular distribution These lesions typically have a high uptake of radioactive tracers on thallium 201 SPECT[66] or fluorodeoxyglucose PET, as opposed to TE. However, diagnosis ultimately depends on a tissue diagnosis.AIDS PCNSL are almost always high-grade, diffuse B-cell lymphomas, often of immunoblastic subtype.

The tumor is treated with cranial irradiation (usual adult dose is fractionated 4000-5000 cGy), and by instituting or optimizing cART. Chemotherapy, if used, typically includes methotrexate, and there are also some positive

results using antiviral therapies (e.g., ganciclovir) that decrease EBV viral load[83] .

Non-Hodgkin's Lymphoma

The other neurological complication of AIDS-associated lymphoma is metastases to the central nervous system by non-Hodgkin's lymphoma. These metastases are typically meningeal rather than intraparenchymal. Neurological disease may herald the tumor, and the latter may remain occult despite repeated lumbar punctures. Affected individuals may present with altered cognitive function, cranial neuropathies, or spinal root lesions, as with meningeal lymphomatosis and carcinomatosis seen in the absence of HIV infection. In addition to repeated cerebrospinal fluid analyses, studies that may prove diagnostically useful include bone marrow biopsy and abdominal CT[6].

Kaposi's Sarcoma

CNS involvement by Kaposi's sarcoma is distinctly unusual.Common signs and symptoms include cranial nerve palsies and polyradiculopathy and less commonly myelopathy due to epidural metastasis with spinal cord compression. Intraparenchymal mass lesions are uncommon[6].

MISCELLANEOUS

Cerebrovascular complications

HIV infected patients are at increased risk for cerebral infarction. A large study of patients with AIDS (n = 1,286) found 1.6% to have cerebrovascular complications[6]. There is a broad spectrum of etiologies, but in many cases the pathogenesis of this is unclear. Cerebral granulomatous angitis due to inflammation in the walls of large and medium sized vessels can result in thrombosis and infarction. Both intracerebral and leptomeningeal arteries may be involved. Varicella zoster infection as well as syphilis may produce cerebral infarction. Nonbacterial thrombotic endocarditis also may be responsible in a number of cases.

CT and MRI may show the sequelae of cerebrovascular disease,including parenchymal haemorrhage, infarction, subarachnoid harmorrhage, and communicating hydrocephalus. Hypodensity is seen on CT, involving both gray and white matter, confined to a vascular distribution. MRI often demonstrated infarction before detection by CT, with increased signal seen on proton density and T2WIs. Enhancement of arterial structures on MRI may indicate sluggish flow and may be an early sign of infarction[84].

MATERIALS AND METHODS

PLACE OF THE STUDY

This study was conducted at the Government Coimbatore Medical College Hospital ,Coimbatore. Patients admitted to the wards of the general medicine, skin & STD and Neurology wards were subjects of the study.

PERIOD OF STUDY

October 2010 to September 2011

DESIGN

Prospective cross sectional study.

METHODOLOGY

All HIV-infected patients who was admitted in medicine, neurology and skin and STD wards CMC Hospital between October 2010 and September 2011 were subjected to thorough neurological evaluation and those with symptoms referring to neurological illness were enrolled in this study after an informed consent.Hospitalised patients with neurological signs and symptoms who were screened based on clinical clues and confirmed to have HIV-1 and/or HIV-2 infection (seropositive) by two HIV test systems

(Rapid / ELISA / Western Blot) were also enrolled. Data was collected in a pretested proforma by meeting the objective of the study. A detailed history, physical findings with thorough neurological examination and necessary investigations were recorded. Treatment and outcome were not included in this study.

INVESTIGATIONS

All patients with neurological symptoms were individualised and were subjected to the investigations listed based on clinical findings. CD4 count was done to all patients.

1. Complete blood count.
2. Renal function test (Sugar, Urea, Creatinine and Electrolytes)
3. Liver Function Test
4. Chest X-ray - P.A View
5. CSF analysis (where not contraindicated) –

    Protein, Glucose, cell count and type,

    AFB, Gram stain, India Ink preparation,

2. VDRL and serology to detect specific infection.

3. Neuroimaging (CT/MRI) where required.

4. Serology to detect antibody to Toxoplasma, CMV and other opportunistic Infections.

5. Nerve conduction studies and EMG where required

METHODOLOGY OF INVESTIGATION

HIV testing and CD4 count were done by microbiology department in our hospital as per NACO Guidelines.

CD4 count was done with Facs Count (Automated Counter) manufactured by Becton and Dickinson.

Tests were done in a single laboratory by the same person, with minimal intrapersonal error.

INCLUSION CRITERIA

Adults presenting with neurological manifestations and diagnosed to be HIV seropositive by following criteria:

1. One rapid test + One ELISA test or

2. Two ELISA or

3. One ELISA + One Western Blot

EXCLUSION CRITERIA

Patients with pre-existing neurological disease

Immunocompromised state due to any other cause and

children<14 yrs of age.

STATISTICAL METHODS EMPLOYED

Following statistical methods were employed in the present study.

1. Contingency coefficient analysis (CC)
2. Chi-square test
3. Independent samples 't' test
4. One-Way ANOVA

All the statistical operations were done through SPSS for Windows, Version 10.0 (SPSS Inc, 1999, New York) (Statistical Presentation System Software).

OBSERVATIONS AND RESULTS

- 170 seropositive HIV patients were hospitalized in CMCH between October 2010 and September 2011.
- 71 patients had neurological manifestations among the 170 patients were enrolled in this study.
- The prevalence of neurological manifestations among hospitalized HIV patients is 41.7%.

AGE AND SEX DISTRIBUTION

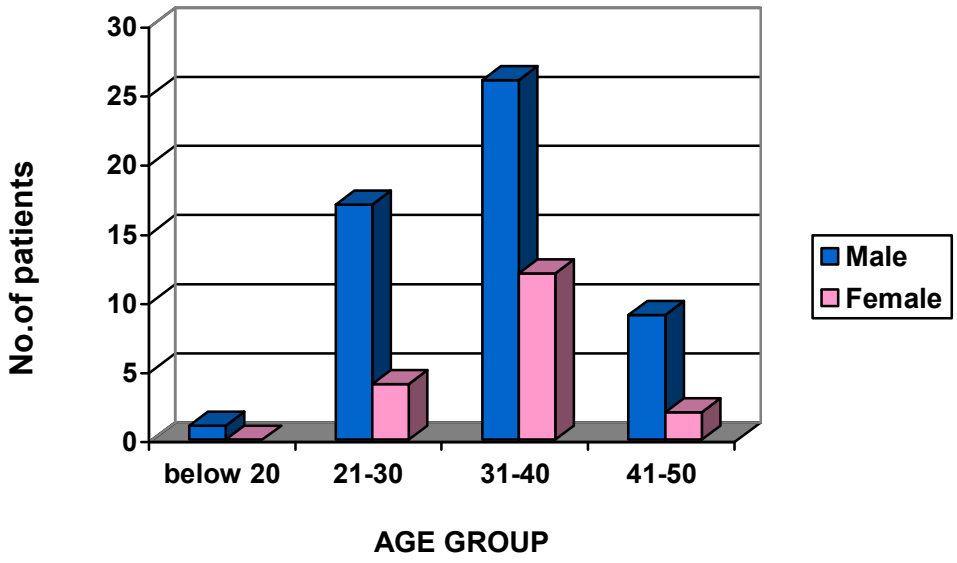
Table: 1 Age * sex cross tabulation

AGE		*SEX*		*TOTAL*
		MALE	*FEMALE*	
BELOW20	COUNT	1	0	1
	% WITHIN SEX	1.9%	0	
21-30	COUNT	17	4	21
	%WITHIN SEX	32.1%	22%	
31-40	COUNT	26	12	38
	%WITHIN SEX	49%	66.6%	
41-50	COUNT	9	2	11
	%WITHIN SEX	16.9%	11.1%	
	TOTAL	53	18	71

- 53 males(74.6%) ; 18 females(25.4%).
- M:F ratio is 2.94:1

- Mean age for males 34.6 yrs; for females 31.1 yrs.
- 92.95% between 15-45 yrs of age.
- Majority of the patients with neurological manifestations in our study were between 31-40 yrs of age (53.5%).

Fig - 2 AGE SEX DISTRIBUTION



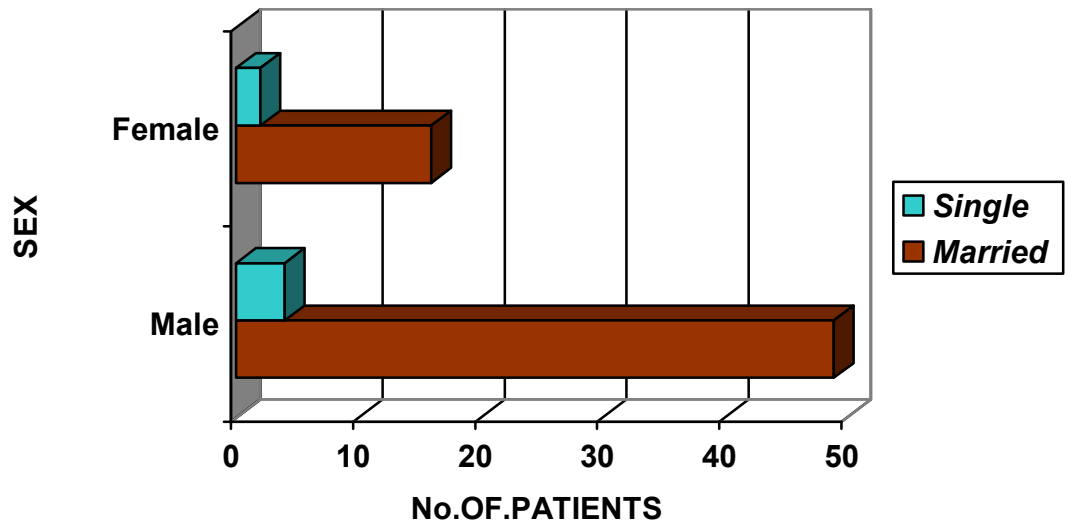
MARITAL STATUS AND SEX DISTRIBUTION

- Only 6 patients were unmarried(8.5%).
- Married 91.5% ; male 49: female 16

Table: 2 Marital status and sex crosstabulation

Marital status		*Sex*		*Total*
		male	female	
Married	Count	49	16	65
	%within sex	92.5%	88.8%	91.5%
Single	Count	4	2	6
	%within sex	7.5%	11.2%	8.5%
Total		53	18	71
		100%	100%	100%

Fig - 3 MARITAL STATUS



OCCUPATION

- In our study most of the patients were daily labourers(26.7%) and Drivers(25.3%).

Table: 3 Occupations involved in this study

OCCUPATION	*MALE*	*FEMALE*	*TOTAL*	*PERCENTAGE*
AGRICULTURE	*6*	*1*	*7*	*9.8%*
DAILY LABOURER	*10*	*9*	*19*	*26.7%*
DRIVER	*18*	*0*	*18*	*25.3%*
HOUSEWIFE	*0*	*6*	*6*	*8.5%*
UNEMPLOYED	*3*	*0*	*3*	*4.2%*
SKILLED WORKER	*5*	*0*	*5*	*7.1%*
UNSKILLED WORKER	*6*	*2*	*8*	*11.3%*
BUSINESS	*1*	*0*	*1*	*1.4%*
OTHERS	*4*	*0*	*4*	*5.6%*
TOTAL	*53*	*18*	*71*	*100%*

- Majority of the patients were from lower socioeconomic class

MODE OF TRANSMISSION

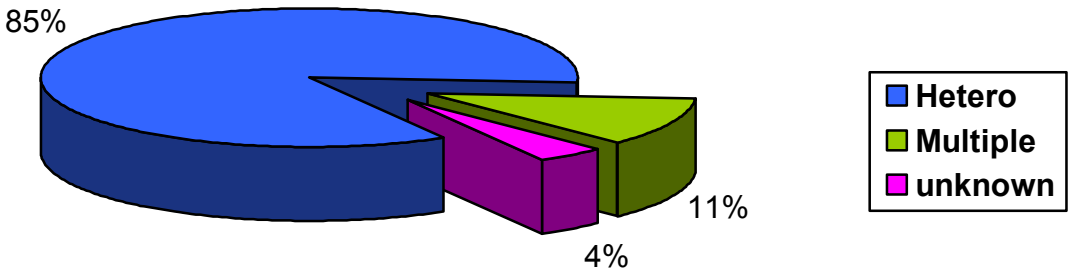
Table: 4 Route of transmission

ROUTE OF TRANSMISSION	*FREQUENCY*	*PERCENTAGE*
HETEROSEXUAL	*60*	*84.5%*
MULTIPLE	*8*	*11.3%*
UNKNOWN	*3*	*4.2%*
TOTAL	*71*	*100%*

- Heterosexual transmission was predominant in most patients.

- The various routes of transmission in multiple transmission group were blood transfusion, surgery and contact with CSW in various combinations.

Fig - 4 MODE OF TRANSMISSION



PRESENTATION: OLD/NEW

Table: 5 Presentation Old/New cases

	FREQUENCY	*PERCENTAGE*
OLD	28	39.43%
NEW	43	60.56%
TOTAL	71	100%

- 39.4% of the cases were diagnosed to have HIV prior to admission.

- Neurological manifestations heralded the onset of HIV in 60.6% of the cases.

NEUROLOGICAL SYMPTOMS

This table shows the various clinical presentations and their frequency in the patients having neurological manifestations.

Table: 6 Neurological symptoms

SYMPTOMS	*FREQUENCY*	*PERCENTAGE*
HEADACHE	48	67.36
ALTERED SENSORIUM	29	40.8%
FND	17	23.9%
SEIZURES	14	19.7%
SENSORY	7	9.8%
BEHAVIOURAL	5	7.0%

- Headache was the commonest symptom (67.3%) fallowed by altered sensorium(40.8%).
- Headache as observed in this study was primarily due to a meningeal infection, tuberculous and cryptococcal meningitis being the most frequent.

Fig - 5 NEUROLOGICAL SYMPTOMS

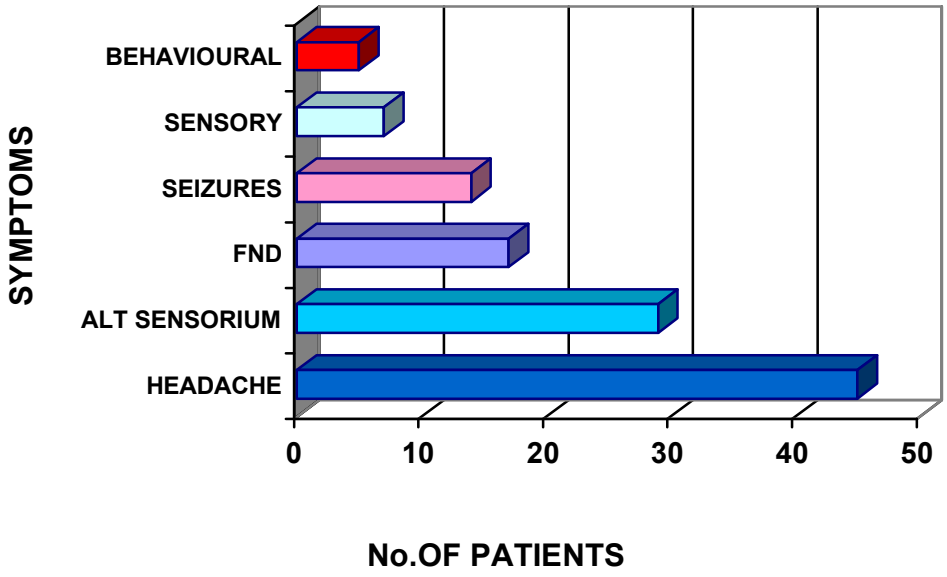


FIG - 6 SHOWS VARIOUS DISEASES PRESENTING AS HEADACHE IN THIS STUDY

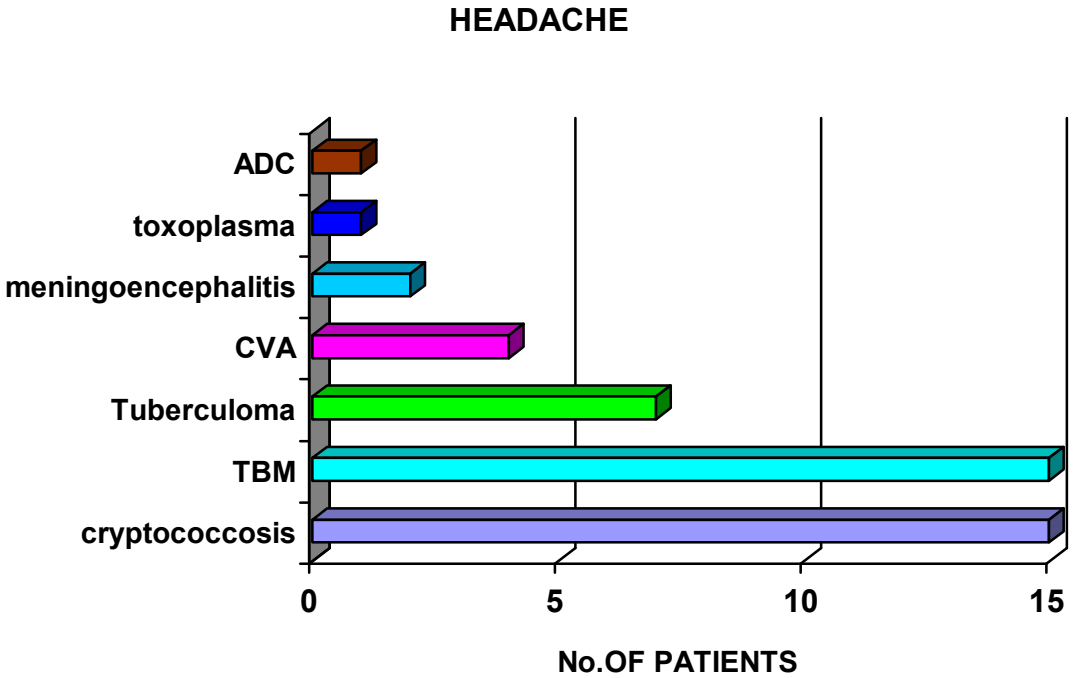


CHART SHOWS VARIOUS DISEASES PRESENTING AS ALTERED SENSORIUM

Fig - 7 ALTERED SENSORIUM

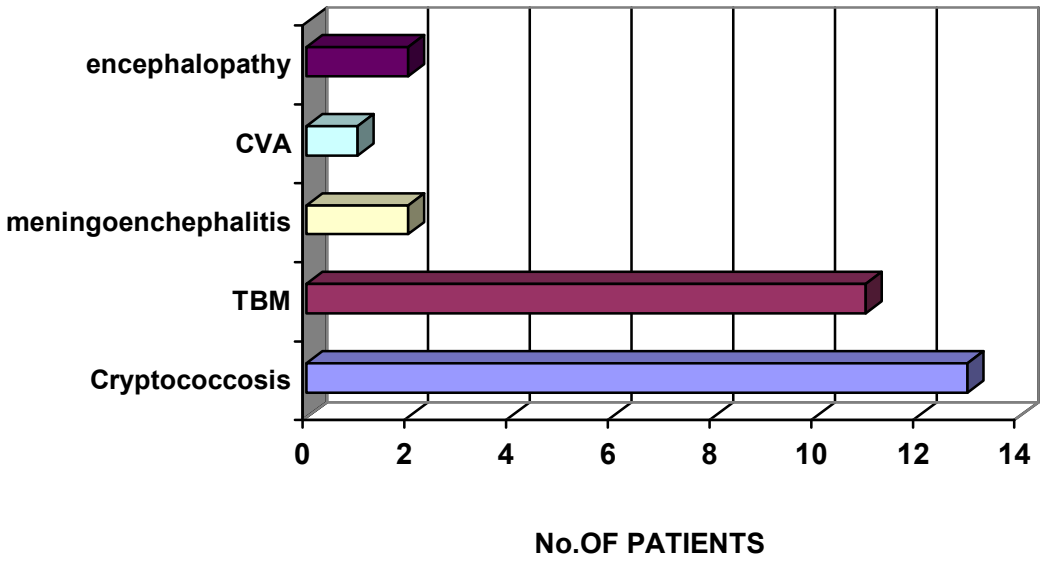
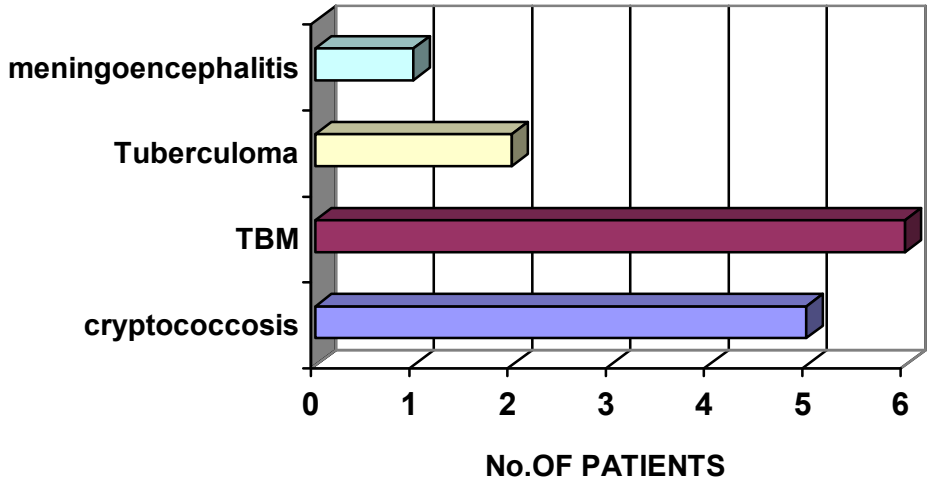


CHART SHOWING VARIOUS DISEASES PRESENTING AS SEIZURES

Fig - 8 SEIZURES



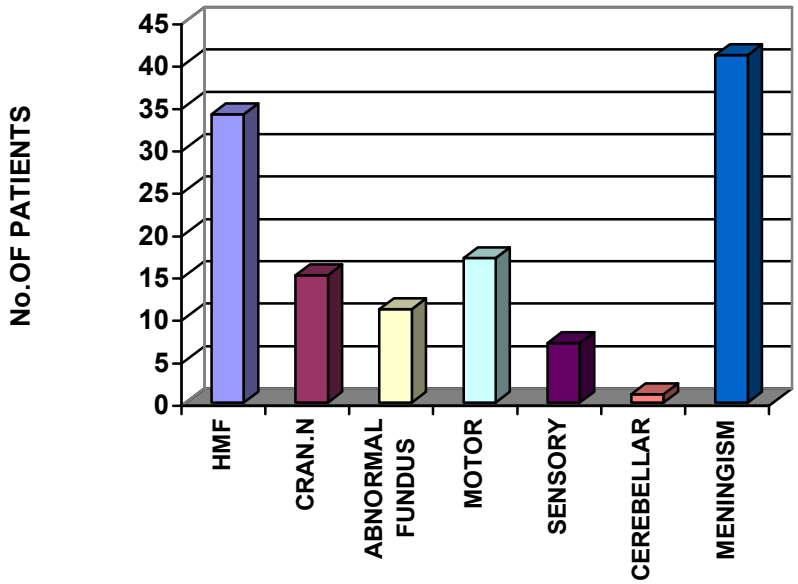
NEUROLOGICAL SIGNS

Table: 7 Neurological signs

CNS SIGNS	*FREQUENCY*	*PERCENTAGE*
HMF	34	47.8%
CRANIAL NERVE	15	21.1%
ABNORMAL FUNDUS	11	15.5%
MOTOR	17	23.9%
SENSORY	7	9.8%
CEREBELLAR	1	1.4%
MENINGISM	41	57.7%

- Signs of meningeal irritation were present in 57.7% of the cases. This includes 15 cases of Cryptococcal Meningitis and 22 cases of CNS Tuberculosis.

Fig -9 CNS SIGNS



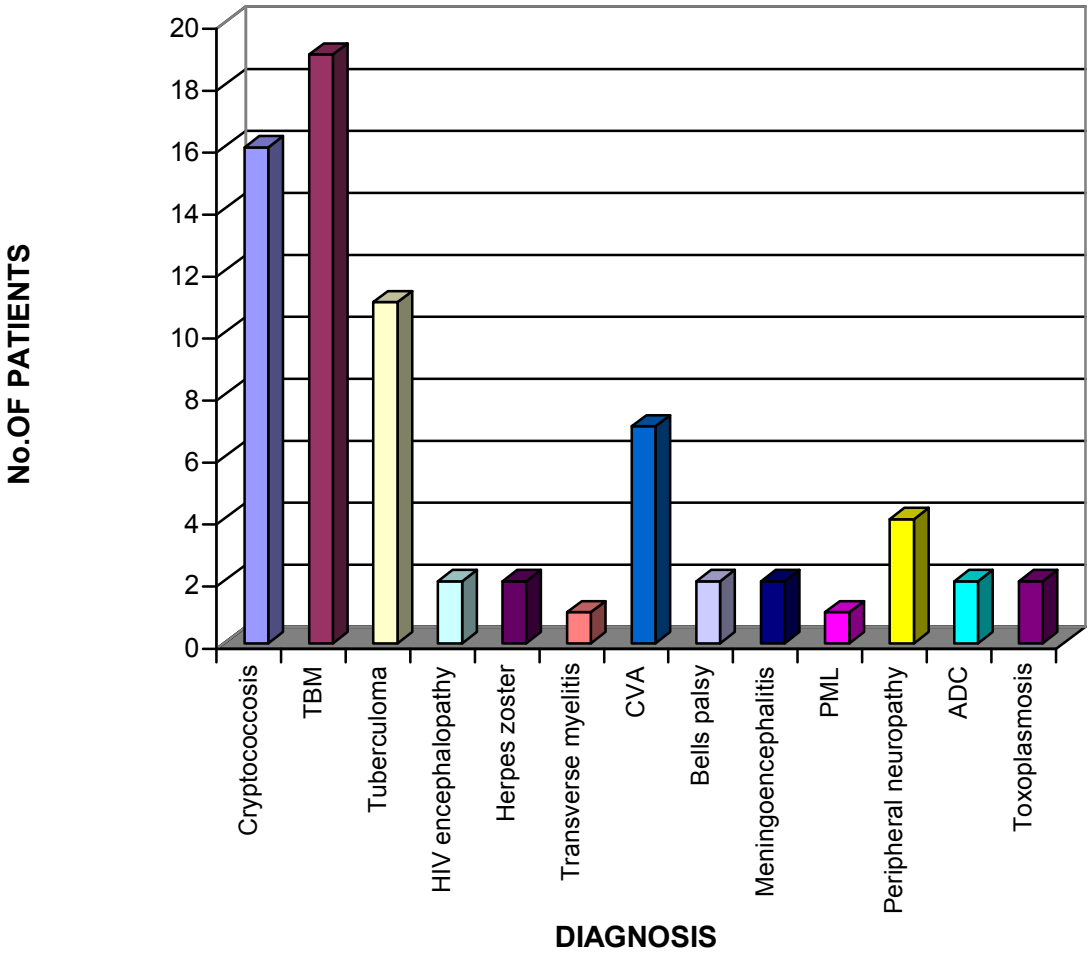
- 40.8% had altered mentation that included 4 patients with cognitive dysfunction
- Cranial nerve involvement was seen in 15 patients

DISEASE PATTERN

Table: 8 Disease pattern

DIAGNOSIS	*FREQUENCY*	*PERCENTAGE*
CRYPTOCOCCOSIS	16	22.53%
TBM	19	26.76%
TUBERCULOMA	11	15.49%
HIV ENCEPHALOPATHY	2	2.81%
HERPES ZOSTER	2	2.81%
TRANSVERSE MYELITIS	1	1.4%
CVA	7	9.86%
BELLS PALSY	2	2.81%
MENINGOENCEPHALITIS	2	2.81%
PML	1	1.4%
PERIPHERAL NEUROPATHY	4	5.63%
ADC	2	2.81%
TOXOPLASMOSIS	2	2.81%
TOTAL	71	100%

Fig - 10 DISEASE PATTERN



- CNS tuberculosis is the commonest disease in patients presenting with neurological abnormalities (42.25%). 11 of these patients had tuberculoma.

- 41 patients presented with meningeal signs.89.5% of TB meningitis and 93.75% of cryptococcal meningitis had features of meningeal irritation.

CD4 COUNT CORRELATION

Table: 9 CD4 count

	CD4 COUNT	
	MEAN	***SD***
PATIENTS WITH NEUROLOGICAL MANIFESTATION	115.1	86.9
PATIENTS WITHOUT NEUROLOGICAL MANIFESTATION	217.7	108.1

- CD4 count levels in patients with neurological symptoms ranged from 12 to 482 with an average of 115.1 .The average CD4 levels in patient without neurological manifestations is 217.7 .there is statistically significant difference between the group (independent group t test p=0.003).

Table: 10 Mean CD4 count levels

NEURO DIAGNOSIS	*CD4 (mean±SD)/micL*
CNS TUBERCULOSIS	97.3± 24.3*
CRYPTOCOCCOSIS	51.6± 22.9*
CVA	116.4± 41.3
TOXOPLASMOSIS	21± 2.8
PERIPHERAL NEUROPATHY	155.5± 26.6*

*p value significant.

Table: 11 CD4 counts in various diseases

DIAGNOSIS	*CD4 COUNT /micL*		
	<100	**100-200**	**200-500**
CCM	*16*	*0*	*0*
TBM	*7*	*12*	*0*
TUBERCULOMA	*6*	*5*	*0*
CVA	*2*	*4*	*1*
PERI.NEUROPATHY	*0*	*3*	*1*
HERPES ZOSTER	*0*	*1*	*1*
TOXOPLASMOSIS	*2*	*0*	*0*
BELLS PALSY	*0*	*2*	*0*
ADC	*0*	*1*	*1*
HIV ENCEPHALOPATHY	*0*	*1*	*1*
MENINGOENCEPHALITIS	*0*	*1*	*1*

Table: 12 CD4 correlation in CNS TB

	No. of cases	*Mean*	*SD*
CNS tuberculosis	30	97.3	24.3
Patients without neurological manifestations	99	217.7	108.1

(p-0.005)

- In this study 16 patients were diagnosed to have Cryptococcal meningitis based on CSF India ink preparation. Mean age 30.8yrs, male: female ratio 2.2: 1.

- The mean CD4 count of patients with cryptococcal meningitis was 51.6± 22.9.

Table: 13 CD4 correlation in Cryptococcal meningitis

	No. of cases	*Mean*	*SD*
Cryptococcal meningitis	16	51.6	22.9
Patients without neurological manifestations	99	217.7	108.1

CSF ANALYSIS

CSF analysis was done in 61 patients.

Table: 14 CSF protein mg/dl

DIAGNOSIS	*N*	*MEAN*	*SD*	*Min*	*Max*
Crypto meningitis	16	139	57.1	32	240
TBM & Tuberculoma	30	199	96.7	74	480
HIV Encephalopathy	2	138	50.9	102	174
Transverse Myelitis	1	206	-	206	206
Meningoencephalitis	2	71	5.6	67	75
PML	1	46	-	46	46
Toxoplasmosis	2	54	3.53	52	57
ADC	2	48.5	7.7	43	54
CVA	5	94	39.2	48	142

Table: 15 CSF cell count per microltr

DIAGNOSIS	*N*	*MEAN*	*SD*	*Min*	*Max*
Crypto meningitis	16	46.91	51.80	10	180
TBM & Tuberculoma	30	267.50	388.36	32	1350
HIV Encephalopathy	2	16.00	13.1	4	30
Transverse Myelitis	1	28.00	-	28	28
Meningoencephalitis	2	16	8.4	10	22
PML	1	0	-	0	0
Toxoplasmosis	2	6	8.5	0	12
CVA	7	10.43	10.1	2	32
ADC	2	1		0	2

· Mean cell count was 140 per microltr, predominantly lymphocytes

minimum 0 cells and maximum 1350 cells per microltr.

· Mean protein and sugar levels were 184 mg/dl and 52 mg/dl respectively.

· Minimum protein level was 32 mg/dl and maximum was 480 mg/dl.

· 25% of the patients had protein more than 200 mg/dl.

IMAGING

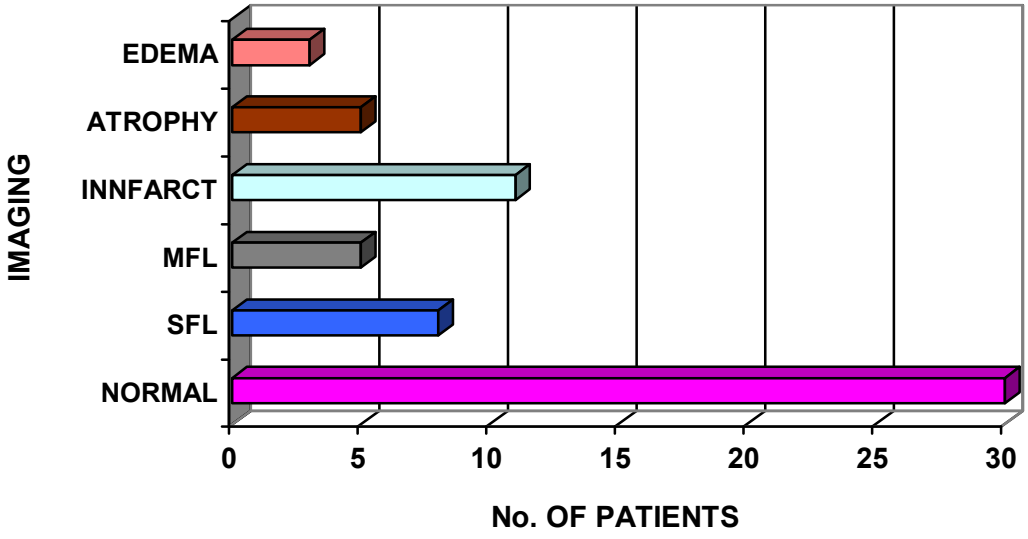
CT BRAIN

Table: 16 CT findings

CT FINDINGS	*FREQUENCY*	*PERCENTAGE*
NORMAL	*30*	*48.3%*
SINGLE FOCAL LESION	*8*	*12.9%*
MULTIPLE FOCAL LESION	*5*	*8.1%*
INFARCT	*11*	*17.7%*
ATROPHY	*5*	*8.1%*
EDEMA	*3*	*4.8%*

- Commonest abnormality was enhancing lesions (31%), ring enhancing in 5 cases and non-ring enhancing lesions in 8 cases.
- 11 patients had infarcts: 3 of TBM, 7 patients had middle cerebral artery infarction, 1 of Cryptococcal meningitis

Fig - 11 CT IMAGING



MRI

- 5 of the patients in this study had MRI brain done for them.2 had multiple ring enhancing lesions who was diagnosed to have Tuberculoma and other 2 patients with multiple focal enhancing lesions diagnosed to have toxoplasmosis.

- One patient had Diffuse white matter high signal intensities and cortical atrophy with ventricular enlargement consistent with a diagnosis of progressive multifocal leukoencephalopathy
- One patient with transverse myelitis MRI spine didn't reveal any abnormality.

FUNDUS

Fundus Examination was done for all co-operative patients. 11 patients had features of papilloedema and no patient had features of HIV Retinitis.

DISCUSSION

In the present study, 71 patients fulfilled the inclusion criteria from about170 patients admitted during study period from October 2010 to September 2011. A prevalence of 41.1% reflects the high prevalence of neurological manifestation in HIV patients.

Neurological complications were seen in 20 % of patients attending the outpatient clinic and in 44.5 % of in-patients in a study by Wadia[85] et al in Pune. In a study by Millogo[86] et al, of the 686 patients admitted 101 (14 %)had neurological manifestation. The incidence of neurological manifestations in HIV positive patients according to snider[5] et al was 31% and levy[6] et al was 39%.

AGE GROUP

The age ranged from 18 to 48 yrs. Mean age was 32 yrs (M 34.6; F 31.1), majority of the patients (92.95%) falling in economically productive age group of 20-45 yrs. Epidemiological analysis of AIDS cases reported to NACO[87] in march 2011 reveals that the disease is affecting mainly the people in sexually active group of 15-44 yrs.

Mc. Arthur et al[7] in their study of 186 patients found the age ranging from 18 to 72 yrs with a mean of 36 yrs for males and 38yrs for females. Snider et al[5] in their study of 50 cases reported the age range from 16 to 69 years in their study group.

Rakenra S[2] et al reported the age ranged from 20 to 65 years, in males, with the mean age being 40.98 ±11.42 years. In females the age was between 23 and 60 years with a mean age of 40.88 ± 11.57 years.

SEX RATIO

Of the 71 patients 53 males(74.6%) ; 18 females(25.4%). M:F ratio is 2.94:1. This gender distribution matches the demography of HIV-1 infection in India (M: F ratio = 3:1)[87].

John et al[88] in his vellore based study observed male to female ratio of 4.26:1.Low figure of female infection rate is due to the admission pattern in most hospitals and social pattern (lifestyle) in our society where females are decreased to household activities and socialize less compared to males.

OCCUPATION

High incidence of neurological manifestations was noted among daily wage labourers (26.7%), followed by drivers (25.3%). Perhaps these patients more

often seek medical help in government hospital and also because HIV infection rate are high in this group of patients.

MODE OF TRANSMISSION

Predominantly heterosexual transmission was observed, (84.5%). Multiple modes of transmission were thought of in 4 patients (11.3%), whereas in 3 patients the exact mode of transmission could not be ascertained. The various routes of transmission in the multiple routes transmission group of patients were blood transmission, surgery and contact with CSWs in various combinations.

Multiple partners and contact with CSWs was the cause of heterosexual transmission, as it is found in other studies in this part of India. (John et al[88] and Deshpande et al[89]). This is in contrast to the western studies where homosexual transmission is more common. (Levy et al[6], Mc. Arthur et al[7]).

The 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.

PRESENTATION

43 patients (60.56%) who presented to us with various neurological disorders were tested to be HIV positive after admission to the wards. The

rest(28) were already diagnosed at the time of admission. Mc. Arthur et al[7] reported that 10% of all AIDS patients in their study presented with complaints referable to the nervous system. Levy at al[6] in their study in San Francisco reported that 1/3 rd of their patients had neurological disorders as their presenting symptoms. Neurological disease is the 1st manifestation of AIDS in 10-20% symptomatic HIV infection[2] .

CLINICAL PRESENTATION

Headache was the commonest symptom seen in 48 patients (63.3%) that included 15 cases of Cryptococcal meningitis and 22 cases of CNS Tuberculosis, followed by altered sensorium in 40.8%, FND in 23.9% and convulsion in 19.7% of the patients.

Amongst other symptoms fever was present in 59% (42) patients that included 13 cases of Cryptococcal meningitis and 24 cases of CNS Tuberculosis, and significant weight loss in approximately 53.5% (38) patients.

Sign of meningeal irritation were present in 57.7% of patients (41) out of these 15 had Cryptococci positive in CSF 17 were diagnosed to have TBM,

5 had tuberculoma (not confirmed by biopsy) and remaining were diagnosed as Meningo-enchephalitis, CVA, encephalopathy.

Cranial nerve involvement was seen in 15 patients. 7 were associated with CVA, two with bells palsy,four with TBM one each with Cryptococcal Meningitis and Herpes Zoster.

Table: 17 Neurological Manifestations comparison

Symptoms/sign (number of patients)	*CCM (n=16)*	*TBM (n=19)*	*Toxoplasma (n=2)*	*CVA (n=7)*	*Tuberculoma (n=11)*
Fever (42)	13(81%)	18 (95%)	1 (50%)	1(14%)	6 (54%)
Headache (45)	15(94%)	15 (79%)	1 (50%)	4(57%)	7(64%)
Focal Neurological Deficit (17)	1(6.3%)	3(15.8%)	0 (0%)	7(100%)	6(54%)
Meningeal signs (41)	15 (93.5%)	17 (89%)	1 (50%)	1 (14%)	5 (45.5%)
Seizure (14)	5 (31%)	6 (32%)	1 (50%)	0(0%)	2(18.2%)
Altered sensorium (29)	13(81%)	11 (58%)	0 (0%)	1(14%)	0 (0%)
Papilloedema (11)	3 (18%)	6 (32%)	0 (0%)	0(0%)	2 (18.2%)

Focal neurological defecit was seen in 17 patients. Of which 12 had hemiparesis, 2 bells palsy and one each of paraperesis and monoparesis.

In the 17 patients with FND 7 was due to CVA, one parapersis due to transverse myelitis and others due to TBM and space occupying lesions.

CD 4 COUNT

- 87.3% of the patients with neurological symptoms had count less than 200.
- CD4 count ranged from 12 to 99 in Cryptococcal meningitis and from 54 to 141 in CNS TB.

CD4 CORRELATION WITH CNS TUBERCULOSIS

There were 19 Patients diagnosed to have TB Meningitis,and 11 patient diagnosed to have tuberculoma The mean CD4 count of patients with CNS TB in the study group was 97.3± 24.3.The mean CD4 count of patients who did not have any neurological manifestations was 217.7. Statistically significant different of CD4 count was observed between the two groups. (P-0.005).

CD4 CORRELATION WITH CRYPTOCOCCAL MENINGITIS

- The mean CD4 count of patients with cryptococcal meningitis was 51.6± 22.9.
- Statistically significant ($p<0.03$) different of CD4 count was observed between the group of patients with cryptococcal meningitis and who did not have any neurological illness.

- Mean CD4 in Cryptococcal meningitis was less than tuberculosis meningitis indicating the occurrence of Cryptococcal meningitis in patients with advance immunosuppresion.

NEUROLOGICAL DISEASE PATTERN

With the advent of HAART the incidence of opportunistic infections decreased remarkably in west with non infectious etiologies leading the list of neurological manifestations. However in countries like India where the prevalence of opportunistic infections is high, it is not surprising to see them leading the list of etiology of neurological conditions[3,4,90] as observed in our study (51/71 i.e. 72%).

Since tuberculosis is the most common opportunistic infection in HIV disease in India, it would be expected to involve the CNS frequently and was the most frequent cause of meningitis in our study. Most Indian studies document tubercular meningitis as being more common than cryptococcal meningitis[85,93].

Table:18 Neurodiagnosis: comparison of various studies in literature

Neurodiagnosis	*Our study % n=71*	*Teja[91] et al n=1606*	*Deshpande[89] et al n=300*	*Throat[92] et al n=102*	*Levy[6] et al n=318*
CNS infections	72	39.4	47	39.22	32.39
Tuberculosis	42.25	25.06	8	5.04	<1
Cryptococcus	22.53	10.95	17	5.99	5.03
Toxoplasma	2.81	9.25	20.33	19.66	5.66
SOL	18.3	27.5	21	0.24	3.45
CMV	---	---	1.33	0.72	11.01
Peripheral neuropathy	5.63	---	8	4.9	7.86
Myopathy	---	---	0.33	---	0
Stroke	9.86	---	7.67	16.6	0.63
HAND	2.81	8.03	1.33	4.9	---
PML	1.4	1.7	6.67	3.9	0.63

CNS Tuberculosis

The commonest neurological complication of HIV infection in this study was due to tubercular involvement of the nervous system. It was seen in 30 patients (42.2%). Of them, 19 had tubercular meningitis, 11 had intracranial tuberculomas. The diagnosis was made based on clinical, imaging CSF

analysis and response to treatment. The mean age at diagnosis was 34.68yrs. Tuberculosis was the presenting manifestation in 13 cases. 4 patients had focal deficits due to vasculitis/mass lesion.

Associated intracranial mass lesions suggestive of tuberculoma are more commonly reported in HIV positive individuals (60% vs 14%) as compared to those with seronegative TBM in a study conducted by Satishchandra[90] et al. In the present study 11 patients(15.49%) had tuberculoma.

Berenguer et al[94] compared clinical features and course of culture proven TBM with and without HIV infection and concluded the HIV infection did not alter the course of the tubercular illness and also response to treatment.

Cryptococcal Meningitis

Meningitis manifested in more than 57 % of the cases. Cryptococcus was the etiological agent in 36.5% of the meningitis cases 15 out of 41. Wadia et al[85] reported meningitis in 17.88 percent of the 457 patients, Cryptococcal meningitis in 67.44 % and tubercular in 18.60 %.

In this study 16 patients were diagnosed to have Cryptococcal meningitis based on CSF India ink preparation. Mean age 34yrs, male: female ratio3: 1.

14 had fever, 15 had headache, and altered sensorium was seen in 13 patients, 5 had convulsions 1 had FND. Signs of meningeal irritation were present in 15 out of 16 cases. Cryptococcal antigen detection and culture was not carried out due to cost constraints and CSF India ink was the diagnostic criteria for all.

Chunk et al[95] found CSF India ink preparation for cryptococci positive in only 50-70% of cases while Fernandes et al showed Indian ink positivity in 55% of cases. Hence a number of patients with Cryptococcal meningitis may have been missed in this study.

Toxoplasmosis

The incidence of toxoplasmosis in different studies has been from 1.33% to 3.3%[3,4,90].The incidence in the present study was 2.81%, comparable to rest of Indian studies.Of the 2 patients one presented with hemiparesis other with fever and headache. Both the patients had low CD4 count 19 and 23. Toxoplasmosis is diagnosed in these patients based on clinical radiological grounds with elevated IgM antibodies. One of the interesting features is that CSF picture was normal in both of our patients.

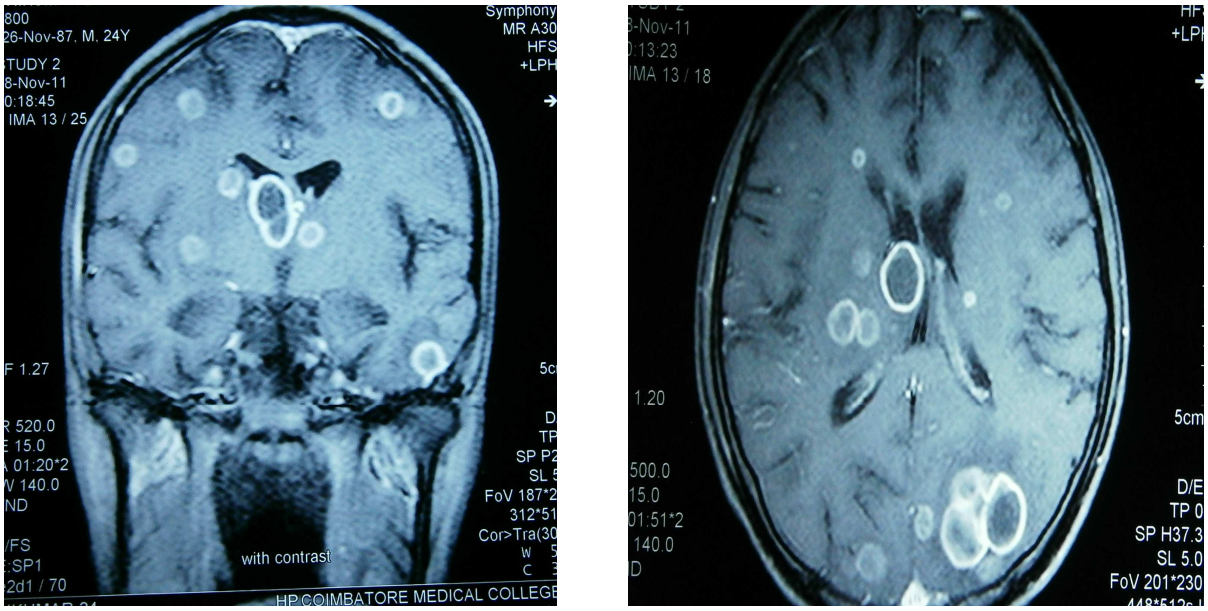


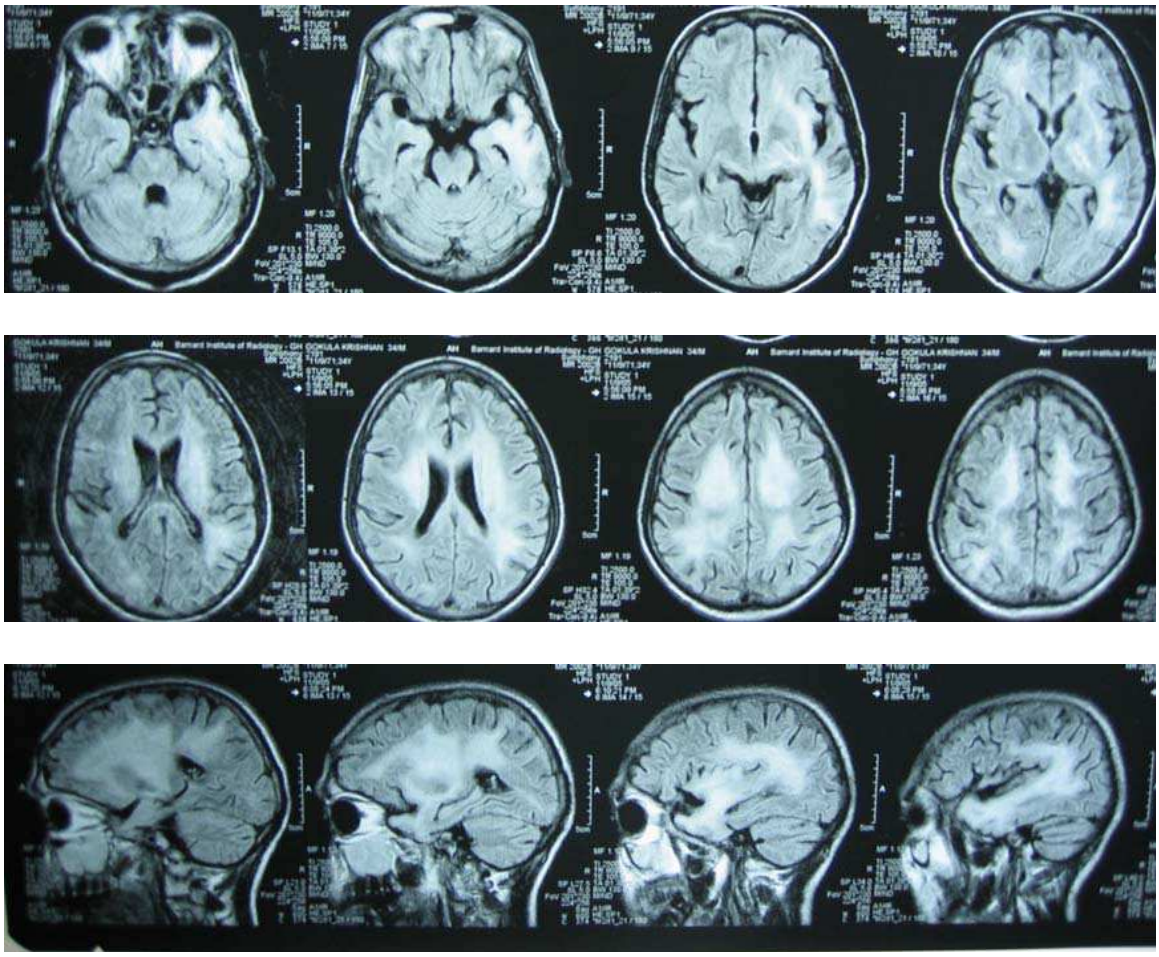
Fig- 12 MRI showing multiple enhancing lesions in Toxoplasmosis

Herpes Zoster

Two patients in our study had Herpes zoster. The diagnosis of herpes zoster was made clinically on the basis of characteristic presentation of vesicles in dermatomal or disseminated pattern. The fist patient had thoracic dermatomal distribution and the second one presented with trigeminal distributon. herpes zoster was presenting disease in the first patient HIV infection detected after hospitalization. The incidence of herpes zoster in HIV infection has been reported to be 11.8% by Das AL et al[96].

Progressive Multifocal Leucoencephalopathy

Fig - 13 MRI Brain showing extensive white matter lesions (PML)



s

One patient in our study was diagnosed to have progressive multifocal leucoencephalopathy (1.4%). The patient had involuntary movements involving right upper and lower limbs with memory loss on presentation. Mini mental score of the patient was 20. C.S.F analysis showed no abnormalities. MRI brain revealed extensive white matter lesions involving

left caudate nucleas, capsuloganglionic region, bilateral parietal and occipital regions, with enhancement on T2W flair image. Snider et al[5] studied 50 patients with AIDS, in which he had 2 patients with progressive multifical leucoencephalopathy.

Meningoencephalitis

Two of our patients presented with acute onset high-grade fever, severe prostration and altered sensorium. CSF analysis was normal. Since no organism could be identified or isolated by routine analysis a diagnosis of viral etiology was made.

HIV Associated Neurocognitive Disorders

Many of the patients in our study had impaired cognitive functions in ranging degrees as seen clinically as well as by psychological testing. However the presence of opportunistic infection was on exclusion criteria for the diagnosis of HIV dementia. Hence only 2 pts (2.81%) 1 males and 1 female were diagnosed to have AIDS dementia complex in this study by psychological analysis and mini-mental scoring system. CSF analysis was normal , with CD4 counts 381 and 189. CT scan showed cerebral atrophy in one patient and normal in other.

Mc. Arthur et al[7] reported incidence of 7.3% in AIDS. They also reported increased incidence in homosexual man and increase with age. R singh et al[2] reported a high incidence of HAD (33.65%). In view of these findings baseline MMSE is probably advisable for all cases with HIV seropositivity and periodic evaluation may unearth more cases with AIDS dementia complex.

Peripheral neuropathy

Peripheral neuropathy was found in 4 patients. Of these 2 patients were on stavudine based ART and two patients were not on ART. Patients with peripheral neuropathy had a mean CD4+ level of 155.5± 26.6 /µl. The predominant manifestations in most were a painful burning sensation in the feet with late and mild involvement of the hands. The patients with peripheral neuropathy had relatively higher level of CD4+ counts compared with patients having other neurological diseases. Nerve conduction studies in these subjects showed distal sensory polyneuropathy.

Bells Palsy

Unilateral infranuclear facial palsy observed in two young men with high risk behaviour. Both the patients were positive for antibodies to human

immunodeficiency virus (HIV). The CD4 count was 190 and 203/microltr. One had persistent generalised lymphadenopathy, but the clinical criteria for the acquired immune deficiency syndrome (AIDS) were not fulfilled. There were no features of generalised neuropathy, and no other cause for facial palsy was evident.

Cerebrovascular events

Seven patients in our study presented with cerebrovascular complications (9.86%). All seven patients presented with hemiparesis and their CT brain showed middle cerebral arterial territory infarct in 5 of the patients and. Two young patients with hemiplegia without any identifiable risk factors had lacunar infarcts in the basal ganglia and the internal capsule.

Deshpande et al[89] has reported 7.67% incidence of CVA in his study with majority of cases due to thrombotic occlusion of large vessels and vasculitis.Thorat et al[92] reported 16.6% of cerebrovascular events. Stroke mechanisms are variable in HIV-infected patients, with a relatively high incidence of vasculitis and hypercoagulability[97]. Cerebral granulomatous angitis due to HIV infection could result in vascular occlusive disease.

CONCLUSION

1. Incidence of neurological illness in HIV infection in our study was 41.7%.
2. Neurological manifestations heralded HIV in 62 % of patients.
3. Heterosexual transmission is the major mode of transmission.
4. Opportunistic infections are still the leading cause of neurological disorders in our population.
5. Meningitis was the commonest manifestation, (>57 %) 41/71 patients comprising of 15 cases of Cryptococcal Meningitis and 17 cases of Tubercular meningitis.
6. Neurotuberculosis is the commonest disease affecting nervous system fallowed by Cryptococcal infection.
7. There is a significant correlation between the levels of CD4 counts and the type of neurological manifestations of HIV infection.
8. Neurological disorders with HIV infection might serve as an indicator for advanced HIV infection, immunosuppression and decreased CD4 counts.
9. Neuropsychological assessment is mandatory for all HIV-positives patients.

SUMMARY

71 patients of the approximately 170 patients admitted in our hospital had Neurological manifestations, prevalence of 41.7%. Patients age ranged from 18 years to 48 years with male: female ratio of 2.94:1. This indicates the High Prevalence of HIV in economically productive age group, and burden to the economy more than 50% of the patients presented late in the disease process indicating the unawareness and social stigma attached to this sensitive subject.

60.56 percent of the patients presented with neurological pathology and were diagnosed to have HIV infection/AIDS thereafter, i.e., neurological manifestation heralded onset of HIV/AIDS in 62 % of the patients in this study.

Meningitis was the commonest Neurological presentation in HIV infection in this study, more than 57.7%.Tuberculosis is the single most common organism affecting CNS(42.2%).Headache, fever and altered sensorium were commonest symptoms in HIV patients with Neurological pathology.

87.3% of the patients with neurological symptoms had CD4 count less than 200.

CSF analysis was useful in diagnosing Cryptococcal Meningitis and providing clue to tubercular pathology.

Cryptococcal meningitis was present in 22.5% of the cases of HIV infection in this study. Headache and fever were commonest symptoms. It occurred late in the HIV infection as indicated by the mean CD4 count of 51.6/cumm.

Only in two patients with multiple mass lesions on cranial CT, anti-Toxoplasma antibody was positive,although it is the commonest cause of space occupying intracranial lesions in western countries.

CNS Lymphoma was not observed in any of our patients.

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PROFORMA

Subject: Neurological Manifestations in HIV patients

By : Dr.P.Monna Mohamed Jaber.

Guide : Dr.S.Veerakesari, MD.

Name : Age :

Sex :

Place : Occupation : Date of

Admission :

Hospital No : Date of

Discharge :

PRESENTING COMPLAINTS :

Past History : Yes /No

Diabetes Mellitus

Hypertension

H/O Tuberculosis

H/O Exposure to a case of tuberculosis

PERSONAL HISTORY :

Marital Status :

Diet : Appetite : Sleep :

Bowel : Bladder :

Habit : Alcohol Yes /No

Smoking Yes /No

Tobacco Chewing Yes No

RISK FACTORS	**YES/ NO**
Heterosexual	
Homosexual	
I.V drug abuser	

GENERAL PHYSICAL EXAMINATION :

Built & Nourishment :

Pallor : Icterus : Cyanosis :

Clubbing :

Pedal edema :
Oral Candidiasis :
Lymph nodes :
Herpes Zoster :
Glossitis :

VITAL SIGNS

Pulse :
Blood Pressure :
Temperature :
Respiratory Rate :
Weight :

NERVOUS SYSTEM EXAMINATION

HIGHER MENTAL FUNCTIONS :

MINI MENTAL STATE EXAMINATION SCORE :

CRANIAL NERVES :

FUNDUS :

MOTOR SYSTEM EXAMINATION : UPPER LIMB

LOWER LIMB

REFLEXES : SUPERFICIAL REFLEXES

DEEP TENDON REFLEXES

CO-ORDINATION :

INVOLUNTARY MOVEMENTS :

SENSORY SYSTEM EXAMINATION :

PRIMITIVE REFLEXES :

SIGNS OF MENINGEAL IRRITATION :

GAIT :

SKULL & SPINE :

PERIPHERAL NERVES :

OTHER SYSTEMS : CVS

RS

PA

INVESTIGATIONS

Hb%: TC: cells/cumm

DC : N- % ; L- % ; E- % ; M- % ; B- %

ESR:

Urine:

Stool:

X-ray chest :

CSF: Cell count and type

Gram stain

AFB

Indian ink preparation for Cryptococci

Protein

Glucose

Chloride

VDRL

CD4 Count:

CT SCAN:

SPECIAL INVESTIGATIONS:

FINAL DIAGNOSIS :

S.no.	Age	Sex	Married/unmrd	New/old	Occupn	MOT	History					examination						
							Fever	Headache	Alt.sens	Seizures	Wt.loss	HMF	C.N	Motor	Sensory	Menings	Gait/cerb	MMSE
1.	44	M	M	O	D	Hs	Y	Y	Y	N	Y	Ab	N	N	N	+	-	22
2.	22	M	M	N	O	Hs	N	Y	Y	N	Y	-	N	Y	N	+	-	27
3.	39	M	M	O	D	Hs	N	Y	N	N	Y	-	N	N	N	-	-	26
4.	23	F	M	N	D.L	Hs	Y	N	N	N	Y	Ab	N	N	N	+	-	23
5.	19	M	U	N	St	Hs	Y	Y	N	N	N	-	Y	Y	N	-	-	26
6.	33	M	M	N	SW	Hs	Y	N	Y	Y	Y	Ab	N	N	N	+	-	21
7.	35	M	M	N	D	U	Y	Y	Y	Y	Y	Ab	Y	N	N	+	-	23
8.	47	M	M	O	Agr	Hs	Y	N	N	N	Y	-	Y	Y	N	-	-	27
9.	34	M	M	N	D.L	M	Y	Y	Y	N	N	-	N	Y	N	+	-	28
10.	32	F	U	N	Agr	Hs	N	Y	N	N	Y	-	Y	Y	N	-	-	25
11.	22	M	M	N	D.L	Hs	Y	N	N	N	Y	Ab	N	N	N	+	-	20
12.	43	M	M	O	D	M	Y	Y	N	N	N	-	N	N	N	+	-	29
13.	39	F	M	N	HW	Hs	N	N	N	N	Y	-	N	N	N	-	-	28
14.	21	M	M	N	D.L	Hs	Y	Y	Y	N	Y	Ab	N	N	N	+	-	21
15.	38	M	M	N	D	Hs	Y	N	N	N	N	-	N	N	N	-	-	25
16.	33	M	M	N	USW	Hs	Y	Y	N	Y	Y	-	N	N	N	+	-	27
17.	26	F	M	N	HW	M	N	Y	Y	N	Y	Ab	N	N	N	+	-	19
18.	32	M	M	O	D.L	Hs	N	Y	N	N	Y	-	N	N	Y	-	-	26
19.	48	M	M	N	D	M	Y	Y	Y	N	Y	Ab	N	N	N	-	-	24
20.	31	M	M	N	USW	Hs	Y	N	Y	N	Y	Ab	N	N	N	+	-	23
21.	26	M	M	N	O	Hs	N	Y	N	N	Y	-	N	Y	N	-	-	26
22.	35	F	M	O	D.L	Hs	Y	N	Y	Y	N	Ab	N	N	N	+	-	21
23.	37	M	U	O	D	Hs	Y	Y	N	Y	Y	-	Y	N	N	+	-	26
24.	25	M	M	N	U	Hs	Y	N	Y	Y	Y	Ab	N	N	N	-	-	20

S.no	CD4	CSF						TOXO Abs	CT/MRI	DIAGNOSIS
		Protein	Sugar	Cellcoun	P	L	India ink			
1.	12	120	68	69	0	100	+	-	normal	Crypto meningitis
2.	127	74	48	250	0	100	-	-	normal	TBM
3.	77	92	56	128	20	80	-	-	MFL	Tubrculoma
4.	44	102	43	132	10	90	+	-	Norm	Crypto meningitis
5.	61	-	-	-	-	-	--	-	Infarct mca lt	CVA
6.	32	132	47	180	10	90	+	-	Norm	Crypto meningitis
7.	111	112	49	342	0	100	-	-	Infarct rt capsular	TBM
8.	147	64	47	8	100	0	-	-	Infarct mca	CVA
9.	54	122	72	189	5	95	-	-	Cereb atrophy	TBM
10.	190	-	-	-	-	-	-	-	-	Bells palsy
11.	38	151	30	136	0	100	+	-	Norm	Crypto meningitis
12.	71	84	23	64	20	80	-	--	SFL	Tuberculoma
13.	121	-	-	-	-	-	--	-	-	Peripheral neuropathy
14.	108	94	41	208	10	90	-	--	Norm	TBM
15.	23	57	45	12	40	60	-	**+ve**	Multiple enhan lesion	Toxoplasmosis
16.	141	104	67	88	25	75	-	-	SFL	Tuberculoma
17.	49	240	39	88	20	80	+	-	Norm	Crypto meningitis
18.	181	-	-	-	-	-	--	-	-	Peripheral neuropathy
19.	276	174	25	4	100	0	-	-	Norm	HIV Encephalopathy
20.	47	202	34	102	30	70	+	--	Norm	Crypto meningitis
21.	147	142	41	6	60	40	-	-	Mca infarct	CVA
22.	112	480	42	304	10	90	-	-	edema	TBM
23.	59	132	41	44	30	70	-	-	SFL	Tubrculoma
24.	51	189	23	72	0	100	-	-	Norm	Crypto meningitis

S.no.	Age	Sex	Married/unmrd	New/old	Occupn	MOT	History					examination						
							Fever	Headach	Alt.sens	Seizures	Wt.loss	HMF	C.N	Motor	Sensor	Menin	Gait/c	MMSE
25.	40	F	M	O	D.L	Hs	N	Y	Y	N	Y	-	N	N	Y	-	-	29
26.	24	M	M	N	D	Hs	N	N	N	Y	Y	-	N	N	N	+	-	23
27.	36	M	M	N	Agr	Hs	N	Y	N	N	Y	-	Y	N	N	-	-	29
28.	37	M	M	O	D	Hs	Y	N	Y	Y	Y	-	Y	N	N	+	-	24
29.	29	M	M	N	D.L	Hs	Y	Y	N	N	N	Ab	N	N	N	+	-	25
30.	33	F	M	O	D.L	Hs	N	Y	Y	N	Y	Ab	N	Y	N	-	-	22
31.	31	M	M	N	D.L	Hs	N	N	N	N	Y	-	N	N	N	-	-	27
32.	42	M	M	O	D	M	Y	Y	Y	Y	Y	-	N	Y	N	+	-	21
33	36	F	M	N	D.L	Hs	N	N	N	N	Y	-	Y	N	N	-	-	23
34.	37	M	U	O	USW	Hs	Y	N	Y	N	Y	Ab	N	N	N	+	-	25
35.	34	F	M	O	HW	Hs	Y	Y	N	Y	N	-	N	N	N	-	-	27
36.	39	F	M	N	HW	Hs	Y	Y	N	N	Y	-	N	Y	N	+	-	22
37.	26	M	M	O	U	Hs	N	N	N	N	Y	-	Y	N	Y	-	-	29
38.	38	M	M	O	D	Hs	N	Y	N	N	Y	-	N	N	N	-	-	17
39.	42	M	M	O	Agr	Hs	N	N	Y	N	Y	Ab	N	N	N	+	-	23
40.	28	M	M	N	SW	Hs	N	Y	Y	N	N	Ab	Y	N	N	+	-	23
41.	36	M	M	N	D.L	M	Y	N	N	N	Y	-	N	N	N	-	-	27
42.	27	F	M	O	D.L	Hs	Y	Y	N	Y	Y	Ab	N	N	N	-	-	25
43.	33	M	M	O	D	Hs	Y	Y	N	N	Y	Ab	Y	N	N	-	-	24
44.	29	M	M	N	USW	Hs	N	N	N	N	Y	-	N	N	N	+	-	28
45.	38	M	M	O	Agr	Hs	N	Y	N	N	Y	-	N	N	N	-	-	27
46.	25	M	M	N	D.L	Hs	Y	N	Y	N	Y	-	N	N	N	+	-	24
47.	36	F	M	O	OS	U	Y	Y	N	N	Y	Ab	N	N	N	+	-	26

S.no	CD4	CSF						TOXO Abs	CT/MRI	DIAGNOSIS
		Protein	Sugar	Cellcoun	P	L	India ink			
25.	482	-	-	-	-	-	-	-	-	Peripheral neuropathy
26.	27	188	29	103	0	100	+	--	Norm	Crypto meningitis
27.	203	-	-	-	-	-	-	-	-	Bells palsy
28.	89	302	42	84	25	75	-	-	Infarct rt occipt	TBM
29.	79	312	52	168	10	90	-	-	Norm	TBM
30.	189	102	37	30	80	20	-	-	Cereb atrophy	HIV Encephalopathy
31.	117	142	65	102	10	90	-	-ve	SFL	Tuberculoma
32.	108	290	38	280	0	100	-	-	Norm	TBM
33.	142	-	-	-	-	-	-	-	Infact mca	CVA
34.	51	192	44	39	20	80	+	-	Norm	Crypto meningitis
35.	131	180	36	68	20	80	-	-	SFL	Tubrculoma
36.	88	380	53	1350	10	90	-	-	Norm	TBM
37.	147	-	-	-	-	-	-	-	-	Herpes zoster
38.	189	43	39	2	100	0	-	-	Atrophy	ADC
39.	35	169	29	58	6	94	+	-	Edema	Crypto meningitis
40.	132	292	43	302	10	90	-	-	Norm	TBM
41.	69	131	61	48	25	75	-	-	Multiple enhanc lesio	Tuberculoma
42.	64	147	34	97	5	95	+	-	Norm	Crypto. Meningitis
43.	51	123	47	32	74	26	-	-	Infarct mca	CVA
44.	109	180	41	40	10	90	-	-	Cereb atrophy	TBM
45.	89	194	38	120	25	75	-	-	SFL	Tuberculoma
46.	47	32	28	10	0	100	+	-	Norm	Crypto meningitis
47.	101	190	44	272	0	100	-	-	Norm	TBM

S.no.	Age	Sex	Married/unmrd	New/old	Occupn	MOT	History					Examination						
							Fever	Headache	Alt.sens	Seizures	Wt.loss	HMF	C.N	Motor	Sensory	Menings	Gait/cerb	MMSE
48.	43	M	M	O	Agr	Hs	Y	Y	Y	N	Y	-	N	N	N	+	-	22
49.	28	M	M	O	D	Hs	N	Y	Y	N	Y	Ab	N	N	N	+	-	21
50.	34	F	M	O	D.L	Hs	Y	Y	N	N	Y	-	N	Y	N	-	-	20
51.	46	M	M	N	O	Hs	N	Y	Y	n	Y	Ab	N	N	N	+	-	26
52.	38	M	M	N	SW	Hs	N	N	N	N	Y	-	Y	Y	N	+	-	24
53.	35	F	M	O	D.L	M	N	Y	N	N	Y	-	N	N	N	-	Y	27
54.	23	M	M	N	D.L	Hs	Y	Y	N	N	N	-	N	N	Y	-	-	29
55.	36	M	M	N	Agr	Hs	Y	N	Y	Y	Y	-	N	N	N	+	-	25
56.	27	M	M	N	D	Hs	N	Y	N	N	Y	Ab	Y	Y	N	-	-	24
57.	41	M	M	O	Busi	Hs	Y	N	N	Y	Y	-	N	N	N	+	-	22
58.	37	F	M	N	O	Hs	N	Y	N	N	N	-	N	N	Y	-	-	30
59.	24	M	M	N	D	Hs	Y	Y	N	N	Y	Ab	N	N	N	+	-	26
60.	38	M	M	N	USW	M	Y	N	Y	Y	Y	Ab	N	N	N	+	-	24
61.	24	F	U	N	D.L	Hs	Y	Y	Y	N	Y	-	N	N	N	-	--	27
62.	37	M	M	N	D	Hs	N	Y	N	N	Y	-	N	N	N	-	-	28
63.	33	M	M	N	SW	Hs	Y	Y	N	N	Y	-	N	N	N	-	-	24
64.	27	M	M	O	USW	Hs	Y	N	Y	N	N	-	N	N	N	+	-	19
65.	34	M	M	O	D	Hs	Y	Y	N	Y	Y	Ab	Y	Y	N	-	-	18
66.	43	F	M	N	HW	Hs	N	N	Y	N	Y	-	Y	Y	N	-	-	21
67.	31	M	M	O	D	U	Y	Y	Y	N	Y	-	N	N	N	+	-	23
68.	21	M	U	N	U	Hs	Y	Y	N	Y	Y	-	N	N	N	+	--	25
69.	34	F	M	N	HW	Hs	N	N	N	N	Y	Ab	N	N	N	+	-	22
70.	39	F	M	O	SW	Hs	N	Y	N	N	N	-	N	N	N	-	-	19
71.	47	F	M	N	D.L	Hs	Y	Y	Y	N	Y	Ab	N	N	N	+	-	22

S.no	CD4	CSF						TOXO Abs	CT/MRI	DIAGNOSIS
		Protein	Sugar	Cellcoun	P %	L %	India ink			
48.	111	250	46	240	10	90	-	-	Norm	TBM
49.	78	292	34	270	0	100	-	-	Norm	TBM
50.	97	171	42	102	25	75	-	-	Mul enhancing les	Tuberculoma
51.	84	132	70	68	0	100	+	-	Norm	Crypto meningitis
52.	103	207	28	250	15	85	-	-	Norm	TBM
53.	111	46	56	0	0	0	-	-	Abnormal	PML
54.	402	206	65	28	30	70	-	-	Normal	Transv myelitis
55.	86	102	45	108	10	90	+	-	Norm	Crypto meningitis
56.	121	97	34	14	75	25	-	-	L mca infarct	CVA
57.	102	212	26	240	10	90	-	-	Cereb atrophy	TBM
58.	381	-	-	-	-	-	--	-	Normal	Herpes zoster
59.	138	232	75	320	15	85	-	-	Infarct lt temp pariet	TBM
60.	112	67	69	10	60	40	-	-	norm	Meningo encephalitis
61.	74	59	34	92	0	100	+	-	norm	Crypto meningitis
62.	149	-	-	-	-	-	-	-	-	Peripheral neuropathy
63.	19	52	28	0	0	0	-	+ve	Multiple ring lesion	Toxoplasmosis
64.	46	271	29	32	0	100	-	-	Norm	TBM
65.	116	104	65	102	10	90	-	-	SFL	Tuberculoma
66.	143	48	68	2	50	50	--	-	Infarct mca R	CVA
67.	38	72	91	68	25	75	+	-	Norm	Crypto meningitis
68.	111	160	37	288	10	90	-	-	edema	TBM
69.	99	99	47	59	0	100	+	-	Infact parietoccipt	Crypto.meningitis
70.	381	54	46	0	0	0	-	-	Normal	ADC
71.	69	292	39	600	0	100	-	-	Norm	TBM

F	- Female
M	- Male
Agr.	- Agriculture
D.L	- Daily Labourer
DRV	- Driver
H.W	-House Wife
St	- Student
SW	- Skilled worker
USW	- Unskiled Worker
D	- Driver
O	- Others
Hs	- Heterosexual
U	- Unknown
M	- Multiple
MMSE	- Mini mental score examination
C.S.F	- Cerebrospinal fluid
Y	- Yes
N	- No
HMF	- Higher Mental Functions.