A DISSERTATION

ON

CLINICAL STUDY OF NEUROLOGICAL MANIFESTATIONS IN HIV

Submitted to
THE TAMILNADU DR. M. G. R. MEDICAL UNIVERSITY
CHENNAI

with fulfillment of the regulations
for the award of
M.D DEGREE IN GENERAL MEDICINE
BRANCH I

GOVERNMENT MOHAN KUMARAMANGALAM
MEDICAL COLLEGE SALEM

MARCH 2008

CERTIFICATE

This is to certify that the dissertation entitled **"Clinical Study of Neurological Manifestations in HIV"** is a bonafide work done by **Dr. S. MANIKANDAN** in **M.D BRANCH I GENERAL MEDICINE** at Government Mohan Kumaramangalam Medical College, Salem, 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 period from January 2006 to July 2007.

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DECLARATION

I solemnly declare that this dissertation **"Clinical Study of Neurological Manifestations in HIV"** was prepared by me at Government Mohan Kumaramangalam Medical College and Hospital, Salem under the guidance and supervision of **Prof. Dr. K.SATHYAMOORTHY, M.D.,** HOD of General Medicine, Govt. Mohan Kumaramangalam Medical College and Hospital Salem.

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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ACKNOWLEDGEMENT

I am extremely thankful to **Dr. P. SHANMUGAM,** M.S., M.Ch., Dean, Govt. Mohan Kumaramangalam Medical College & Hospital, for allowing me to utilize the hospital facilities for doing this work.

I express my deep sense of gratitude and indebtedness to **Prof. Dr. K.SATHYAMOORTHY**, M.D., Professor & Head of the Department of Medicine, for giving me inspiration, valuable guidance and help in preparing this dissertation.

My sincere thanks to **Dr. K. THIRUVARUTCHELVAN, M.D., D.M.,** Asst. Professor of Neurology, for guiding me in the technical and clinical aspects during each and every step of this study.

I express my deep thanks to **Dr. V. DHANDAPANI,** M.D., for his kind suggestions.

I thank all medical unit chiefs **Prof. R. ANBALAGAN, Prof. T. SUNDARARAJAN, Prof. P. KANAGARAJ, Prof. P.VIJAYARAGHAVAN** for their advices and kind helps.

I thankful to **Dr. L.ARUNACHALAM, M.D.,** and **Dr. T. CHENTHAKRISHNA, M.B.B.S.,** ART Centre, Govt. Mohan Kumaramangalam Medical College Hospital, Salem for the help rendered.

I would also like to thank **Dr. S.R. SUBRAMANIAN, M.D., Dr. D. VIJAYARAJ, M.D., Dr. A. RAVI, M.D., Dr. S.SIVAKUMAR, M.D., Dr. C. BALAMURUGAN, M.D.,** Asst. Prof. of Medicine, for their expert assistance in this study.

My thanks are also due to **A.P. BAGAVATHI** and **V.P.JANARTHANON** for the neat execution of this dissertation.

And finally with great happiness, I thank all patients for their sincere co-operation extended to me throughout the study.

CONTENTS

INTRODUCTION

The acquired Immuno Deficiency Syndrome (AIDS) caused by a retrovirus variously termed Human Immuno Deficiency Virus – 1 (HIV-1) Human T-Lymphocytic Virus III or Lymphadenopathy associated virus is no longer a rare or exotic disease.

Since its first description in June 1981 it is now a Worldwide Pandemic. In the early years of epidemic, nervous system involvement was not widely recognized. It is now recognized that were level of neuraxis can be involved and at least one third of patients with advanced HIV infection will develop neurological complications during the course of their illness and 10% of cases neurological problems may be first sign of development of AIDS. But at autopsy, more than 80% of patients show evidence of cerebral pathology ranging from HIV encephalitis, opportunistic infections or lymphomas and some evidence of peripheral neuropathy.

Neurological manifestations of HIV consists of CNS complications caused directly by HIV, and include cognitive disorders

and other CNS disease such as myelopathy and the demyelinating neuropathies, and the secondary disorders caused by opportunistic infections, neoplasm, cerebrovascular events, as also the effects of metabolic derangements and medications.

Considering the protean manifestations of neurological illness in HIV infected, an analysis of neurological manifestations in this subset of Patients was made.

AIM OF THE STUDY

To study the spectrum of neurological manifestations in HIV infected subjects at various level.

To study the correlation of neurological manifestations with CD_4 count in these subjects.

REVIEW OF LITERATURE

Clinical Disease of Nervous System Accounts for a Significant Degree of Morbidity in High Percentage of Patients with HIV Infection Pucconi (15%), 1989; Wadia (20%), 2001; Vijay Teja (36%), 2005. It is both debilitating and life threatening Neurological complications typically occur with advanced disease and profound Immunosuppression. Autopsy Studies of HIV Disease clearly shows pathological abnormalities of Central Nervous System is around 60-75% (K.S. Shankar, Anita et al., 2002).

Neuropathogenesis:

HIV- Infected individuals can experience a variety of neurological abnormalities due either to opportunistic infections and neoplasm (or) to direct effects of HIV or its products.

Main cell types infected in brain are the perivascular macrophages and microglial cells.

Precise mechanism of HIV enters the brain by induce adhesion molecules such as E-selectin and vascular cell adhesion molecule (VCAM-1) on brain endothelium. HIV gp 120 enhances expression of Inter Cellular adhesion molecule (ICAM – 1) in glial cells. They promote syncita formation. Virus isolation from brain is R5 strains.

HIV infected individuals may manifest white matter lesions as well as neuronal loss. Viral proteins gp 120 and tat trigger release of endogenous neurotoxins from macrophages and astrocytes.

HIV – 1 nef and tat induce chemotaxis of leucocytes and release of neurotoxins from monocytes. Macrophage Derived Neurotropic Factor (MDNF-1) to kill neurons via N-Methyl D-Aspartate receptor. gp 120 infected monocytes cause neurotoxicity by Antagonise vascular peptides.

Monocyte derived cytokines TNF-α, IL-1, IL-6, TGF-β, IFN-γ, Platlet Activating Factorand Endothelin contribute neurotoxic effects. Increased production of Eicosanoids, Nitric Oxide and Quinolinic Acid contribute to Neurotoxicity.

Astrocyte derived IL-6 induce HIV expression in infected cells and down regulate macrophage produced neurotoxins. HIV infected individuals with E4 allele for apoE increased risk for AIDS encephalopathy and peripheral neuropathy.

Primary HIV Infection of the Brain

HIV-1 associated dementia complex

An AIDS-Defining illness, most HIV-infected patients have some neurologic problem during the course of their disease. Incidence of HIV Dementia Central of Disease Control (7%), 1996; Balakrishnan (10%), 1989; Baller et al (7-14%), 2001.

Brain Atrophy characterized by sulcal widening, ventricular dilatation and meningeal fibrosis observed at autopsy in patients with HIV dementia. With advanced immunosuppression, HIV Dementia present as sole manifestation.

Features include disturbed intellect, fatigue, malaise, Headache, loss of sexual drive. Increased forgetfulness, difficulty concentrating,

problems reading and slowness at wide variety of tasks (Navia et al. 1986).

Physical examination reveals Hallmark of advanced AIDS, wasting, alopecia, sebborheic dermatitis and generalized lymphadenopathy. The patient exhibits slow mental processing (Brady Phrenia), abnormalities of saccadic and pursuit movements, diminished facial expression, hypophonia, impaired co-ordination, balance and tremor.

CSF shows mono nuclear pleocytosis in $1/5^{th}$ of individuals, $2/3^{rd}$ have increased protein – 200 mg/μl; oligoclonal band frequently noted (KATZ et al, 2001). Recently HIV p24 Ag, β2-microglobulin, neoptrin and calprotectin (2%) (Dunlop et al., 1991) are demonstrated in CSF in patients with HIV dementia.

CT brain shows brain atrophy, (Central and Contical patterns); MRI shows “punctate” lesion. EEG and other Electrophysiological studies not helpful. The recent studies shows (SCHMITT et al, 2000) HIV dementia improved with high doze of Zidouvidine.

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.

JJ Siditis and Price, 1997 – staging system of HIV Dementia used in both clinical and research areas.

Severity Scales of Dementia

Stage	Dementia
0	Normal mental and motor function. Neurological signs are within the normal age - appropriate spectrum.
0.5	***Equivocal or subclinical:*** Absent, minimal, or equivocal symptoms without impairment of work or capacity to perform ADL. Examination may be normal mildly abnormal; signs may include reflex changes (e.g. generalized increase in deep tendon reflexes with active jaw jerk, snout or glabellar sign) or midly slowed ocular movements, but without clear slowing of extremity movements or loss of their dexterity or strength.
1	***Mild:*** Able to perform all, but the more demanding aspects of work or ADL but with unequivocal evidence (symptoms or signs including performance on neuropsychologic testing) of intellectual or motor impairment. The abnormal motor signs usually include slow or clumsy movements or extremities.
2	***Moderate:*** Able to perform basic activities of self care at home but cannot work or maintain more demanding aspects of daily life (e.g. maintain finances, read text more complex than a tabloid newspaper)
3	***Severe:*** Major intellectual incapacity (cannot follow news or personal events, cannot sustain complex conversation, considerable slowing of all output or motor liability.
4	***End Stage:*** Nearly vegetative. Intellectual and social comprehension and output are at a rudimentary level. Nearly or absolutely mute.

Aseptic Meningitis:

Pullioni et al, (1989) reported 2 cases of Aseptic meningitis in 44 patients. Rosenbaulm et al (1988) reported 21 cases with aseptic meningitis.

Aseptic meningitis seen in any but very late stages of HIV infection. In acute primary infection – syndrome of Headache, photophobia and meningismus are present cranial nerve involvement, predominantly VII and occasionally V / VIII.

CSF shows lympocytic pleocytosis, elevated protein level and normal glucose level. This spontaneously resolve with in 2 to 4 weeks; it is rare following the development of AIDS.

Neuromuscular Disorders

Prospective neurological examination of patients with advanced AIDS will reveal evidence of peripheral neuropathies in as many as 50% (Berger et al, 1994). Peripheral neuropathies occurring with HIV infection are diverse. HIV mediated, immune mediated, infections (CMV, HZV, Syphillitic, Mycobacterium avium complex); nutritional (Vit-B12; Folate deficiency); Toxicity of the therapeutic drugs,

notably dideoxyinosine (ddI), dideoxycytidine (ddC) and stavudine (d4T) are responsible for increasing number of cases of neuropathy.

Four types of neuropathy are important to recognize, either because of their high prevalence or their therapeutic implications, or both. They are

1. Distal symmetric polyneuropathy (DSPN)
2. Mononeuropathy multiplex
3. Inflammatory demyelinating polyneuropathy
4. Progressive polyradiculopathy.

SN Pujari et al (2001) from India reported 17% cases in his series, depending on the study population and the method of case ascertainment, clinical, electrophysiologic or pathologic evidence of peripheral neuropathy is present in about one - third to nearly 100% of patients with advanced HIV disease. The incidence of neuropathy increases with declining CD4 cell count and advancing systemic HIV disease.

Distal symmetrical Sensorimotor neuropathy

Develops generally in late stage of disease in about 30% of patients. Identical presentation of sensory neuropathy seen with dideoxyinosine (ddI), dideoxycytidine (ddC) and stavudine (d4T); patient had painful paraesthesias, dysesthesias and spontaneous pain in feet.

Distal weakness, imparted vibration sense and hyperalgesia frequently detected. The most common signs of DSP in AIDS are depressed or absent reflexes at ankles, relative to the knees. The presence of hyperactive knee reflexes and depressed ankle reflexes may indicate concurrent myelopathy and neuropathy which is a common association in HIV infected individuals. Vibratory thresholds are increased, and pinprick and temperature are reduced in a stocking and glove distribution, whereas joint position sensation is relatively normal. Weakness is generally restricted to intrinsic foot muscles, unless DSP is very advanced, or other neurologic disorders are also present.

Nerve conduction study shows decreased sensory potentials; neurophysiological studies suggest demyelination; nerve biopsy (Sural nerve) shows epineural and endoneural inflammation.

Symptomatic theraphy helpful including combination of Tricyclic and Carbamazepine, but non reverse primary disorders.

Inflammatory demyelinating polyneuropathy

Both acute Gullian-Barre syndrome and Cronic inflammatory demyelinating polyradiculopathy occur with HIV infection. Both are rare and tend to occur in patients with early in stage of their HIV infection with immunological status is fairly well preserved (Simpson et al., 1992).

Acute Inflammatory Demyelinating Polyneuropathy (AIDP) is characterized by rapidly progressive weakness in distal and proximal muscles of two or more limbs associated with generalized are flexia. Occasionally, bilateral facial weakness may be the presenting symptom. The clinical progression of Acute Inflammatory Demyelinating Polyneuropathy (AIDP) is usually rapid and reaches its peak within the first 4 weeks of neurologic illness, with involvement

of respiratory muscles in the most severe cases. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is distinguished by a more slowly progressive clinical course that may be monophasic or relapsing over several months.

Nerve conduction study show features compatible with demyelinating neuropathy. CSF examination reveals normal to increased protein 200 mg/dl with mono nuclear pleocytosis (50 or more cells /μl), a differentiating feature from HIV seronegative Gullian-Barre Syndrome or Chronic Inflammatory Demyelinating Polyradiculopaty.

In contradiction to typical Gullian-Barre syndrome a CSF cytoalbuminocytological dissociation occurs only in minority of affected AIDS patients (Behar R, 1987).

Plasmapheresis and I.V. Immunoglobulin may be associated with striking improvement.

Mononeuritis Multiplex (MM)

Rarely observed with HIV infection, cranial, peripheral or spinal nerves many be affected (Simpson et al., 1992). This disorder is usually attributed to immune complex deposition resulting in a necrotising vasculitis.

Other casues of similar clinical picture, Herpeszoster, cytomegalovirus and lymphmatous nerve root infiltration must be considered in differential diagnosis.

Patients with Mononeuritis Multiplex (MM) have asymmetric or proximal involvement of peripheral nerves and preservation of tendon reflexes in asymptomatic distributions. The typical neurologic presentation includes multifocal sensory and motor abnormalities in the distribution of cutaneous nerves, mixed nerves and nerve roots. Cranial neuropathies are also a frequent feature of Mononeuritis Multiplex (MM).

Signs of focal or asymmetric multifocal axonal lesions and Electrodiagnositic abnormalities (Britton, Lange et al, 1987).

Progressive polyradiculopathy

This is due to cytomegalovirus. Which it recognized early may be treatable and reversible with Gancillovir or Foscarnet.

The clinical presentation of in characterized by radiating pain and parasthesias in the caudaequina distribution, followed by rapidly progressive flaccid paraparesis, lower extremity areflexia and mild sensory loss and sphincter dysfunction. The upper extremities may be involved late in the course of polyradiculopathy. The CSF findings in most patients with progressive polyradiculopathy are characterized by marked polymorphonuclear pleocytosis, elevated protein and cultures are positive for CMV in about half of the patients. The most prominent electrophysiologic abnormalities in Progressive Poly Radiculopathy (PP) are widespread denervation in lower extremity and lumbar paraspinal muslces, accompanied by abnormal late responses in affected distributions. In most cases Progressive Poly Radiculopathy (PP) has a poor prognosis if untreated, with a mortality rate of nearly 100% and a mean duration of illness from onset of neurologic symptoms to death ranging from 2 to 30 days.

Myopathy

Numerous cases of HIV associated myopathy were reported by several groups (Bender, 1998; Carson, 1991). Polymyositis characterized by proximal muscle weakness, myalgias, excessive fatigability and increase in serum creatine kinase. Fibrous tissue proliferation, necrosis and phagovytosis of muscle fibres, accompanied by an intense inflammatory infiltrates are observed in Histopathalogical Examination of involved muscles (Foveretto et al., 1991).

Prolonged use of Zidouvidine therapy results in myopathy. The illness characterized by severe myalgias, proximal weakness and muscle wasting, often striking involvement of Gluteal muscles and following treatment with high doses of drug for 6-18 months. This due to interfere with function of mitochondrial polymerases. Red ragged fibres are histologic hall mark of Zidouvidine induced myopathy. This is reversible following discontinuation of drug.

Spinal cord disorders

Vacuolar myelopathy (VM)

The most common spinal cord disease complicating HIV infection is HIV associated vacuolar myelopathy. The pathologic finding of noninflammatory vacuolation of myelin, particularly in the lateral and the posterior columns of the spinal cord, characterizes VM. Upper thoracic cord is affected most commonly, but cervical pathology is well described and occasionally diffuse cord changes are seen.

The clinical features of HTV–1 related VM have been systematically studied. In an autopsy based clinicopathological correlation, Dal Pan et al found that 15 of 56 patients with pathologically confirmed Vacuolar Myelopathy had clinical evidence of myelopathy. Mild to moderate limb weakness were present in all cases, with severe weakness limited to the most advanced cases. Knee hyperreflexia was common as were lower limb spasticity (eight of 15, 53%) and gait spasticity (60%). A sensory ataxia was seen in 20% of cases. A coexistent distal sensory neuropathy with ankle areflexia or hyporeflexia was also common (eight of 15,53%). A discrete thoracic sensory level was seen in two of 15 cases (13%). Vibration and

position sense loss were common. Bowel and bladder dysfunction were seen in only one case. In all cases, the development was slowly progressive, with onset of symptoms ranging from 3 to 16 weeks before the diagnosis of myelopathy. The development of symptomatic myelopathy is more frequent in patients with pathologically more severe VM.

INTRACRANIAL OPPORTUNISTIC INFECTIONS

Toxoplasma gondii

Central Nervous System toxoplasmosis now represents the most common focal brain lesion in patients with AIDS and possibly the most common opportunistic infection (Synder H.S. et al, 1989). But its incidence is decreasing in era of HAART.

It is most common from France and Caribbean. In patients with AIDS, over 95% of toxoplasmic encephalitis is due to reactivation of a chronic (latent) infection. For most HIV infected patients, toxoplasmic encephalitis (TE) develops when the CD4 + T lymphocyte count CD4T count) falls below 100/mm3.

It is 10 times more common in patients with antirodies to organism than seronegative. Most Toxoplasmosis in the AIDS patient is most frequently manifested by toxoplasmic encephalitis, usually alone or less frequently as part of multiorgan infection. Isolated organ involvement without CNS disease is uncommon, TE most frequently presents (50 to 89%) with a subacute onset of neurological deficits with or without evidence of generalized cerebral dysfunction. Less often (15 to 25%), seizures may be the initial manifestation. The clinical presentation varies from an insidious process evolving over several weeks to a more acute, at times fulminant course. Abnormalities associated with focal lesions include hemiplegia, hemisensory loss, hysphasia. aphasia, movement disorders (hemichorea and hemiballismus), ataxia, diplopia cranial nerve palsies, cerebellar tremor, severe localized headache, Parkinsonian syndrome, and intractable hiccoughs. Abnormalities attributable to generalized cerebral dysfunction include lethargy, confusion, coma and global cognitive impairment similar to AIDS related dementia.

MRI shows multiple lesion in multiple location (Balakrishnan et al, 1994). These lesion exhibit inflammation and central necrosis, as a

result demonstrate ring enhancement on contrast MRI (Becker P.S. et al., 1995).

In double contrast CT evidence of surrounding edema present (Kumar et al., 1995).

In addition to Toxoplasmosis, the differential diagnosis of single or multiple enhancing mass lesion in HIV infected patients includes primary CNS lymphoma, TB or Fungal or Bacterial Abscess (Calzada Lopaz et al., 1994).

Definitive diagnosis is Biopsy.

In CSF analysis, free extracellular tachyzoites, and CYST forms identified with wright straining of cytocentrifuge preparations (Dement S.H. et al., 2003).

CSF shows low glucose (20 mg/dl) persisted for 10 days. (Cox et al., 2002). Cytocentrifuge, Wright stain superior to multipore filter papanicolaou stain preparation (Gupta et al., 2004).

Cryptococcus neoformans

This is extraordinarily common in AIDS patients, with reported incidence varying Wadia (2001), (34%), Levy (1989) (41%), Koppel (47%), Recart (2001) (39%).

Afro-Americans and I.V. Drug Abusers at increased risks.

Persistent head ache (universal complaint), Nausea, vomiting, mental status changes, photophobia, blurred vision, fever, meningismus also common. Less frequently observed are cranial nerve palsies, Hemiparesis, Language disturbances, seizure, cerebellar degenration and psychosis.

Typical locations are Brainstem and Basal ganglia. Intracranial pressure elevation and sudden clinical deterioration from Herniation are common. Pathological examination reveals a basilar, chronic meningsis that is neither thick nor exudative.

Diffuse or focal opacifications of leptomeninges, small nodules and cystic lesion composed of clusters of budding yeast with reactive gilosis in basal Ganglia.

The CT of the head is normal or shows cerebral atrophy in 75 to 90% of cases. Non-enhancing and contrast enhancing lesions presenting as either nodular or ring like patterns, particularly in the basal ganglia are seen. CSF can be normal or show mononuclear pleocytosis, elevated protein, low glucose and high opening pressure. India ink preparations are positive in 72 to 88% of patients. Determination of CSF Cyptococcal Antigen (CRAG) titre is essential because this may be the only CSF abnorrmality; latex agglutination of CSF for Cryptococcal antigen has a sensitivity of 91% to 100%. A positive CSF culture is the definitive diagnostic test for Cryptococcal meningitis and the main entry criteria in published series. Being the gold standard, its sensitivity approaches by definition 100%.

Mortality rate with cryptococcal meningitis high. This is due to elevated intracranial pressure.

Other Fungal Infections

In addition to cryptococcal meningiits, other CNS fungal infections such as Histoplamosis, Coccidioidomycosis, Blastomycosis and Aspergillosis have been reported.

Progressive multifocal leucoencephalopathy (PML)

Progressive multifocal leucoencephalopathy (PML) is a demyelinating disease of the central nervous system that results from infection of oligodendrocytes with JC virus, a papovavirus. It affects approximately 4 to 8% of patients with advanced HIV disease. It is a subacute or chronic progressive illness most often characterised by focal neurologic findings such as hemiparesis, gait abnormalities and visual field cuts, and mental status and personality changes. Dementia, encephalopathy and coma can occur with fulminant disease, Seizures are uncommon, but not rare.

Radiographic imaging provides the strongest support in diagnosing Progressive multifocal leucoencephalopathy (PML) but presently confirmation requires brain biopsy. Affecting the white matter, generally not enhancing with contrast and exhibiting no mass effect, the hypodense lesions of PML on CT of the brain reveal areas that may have a “scalloped” appearance as a result of the subcortical fibers lying beneath the cortex. The lesions have a predilection for the frontal and parieto-occipital lobes, may occur virtually anywhere. The brainstem or cerebellum may be solely involved in upto 15% of cases.

Demyelination observed with HIV associated dementia may be radiographically indistinguishable from that of Progressive multifocal leucoencephalopathy (PML). Clinically however PML is associated with focal neurological disease and is much more rapidly progressive. Radiographic distinctions include a greater propensity of lesions to involve the subcortical white matter, its hypointensity on T1 weighted images and its rare enhancement.

Routine CSF evaluation is nondiagnostic and is usually normal or reveals only nonspecific changes such as mild pleocytosis or protein elevation. CSF PCR detection of JC virus DNA has become the successful tool in the diagnosis of PML.

Viral encephalitis

Herpes simplex virus typically cause acute hemorrhagic necrotizing encephalitis with predilection for subfrontal and medial temporal lobes. In AIDS patients HSV encephalitis presents with typical clinical features which include headache, fever and variable combinations of seizures, behavioral and cognitive changes, focal signs and ultimately obtundation. Definitive diagnosis often requires

brain biopsy, but CSF PCR would reduce the need for tissue diagnosis.

Herpes Zoster virus

Herpes zoster virus infection of the nervous system may result in radiculitis. characterized by painful vesicular cutaneous eruptions involving one or several dermatomes. It also causes subacute encephalitis in a number of AIDS patients with clinical features which include lethargy, confusion and variable focal findings including cranial neuropathies. Myelitis due to herpes zoster had been described in imunocompromised patients including AIDS patients with clinical features such as subacute progression of motor weakness, sensory deficits and sphincter disturbances in varying combinations that evolve over weeks.

Cytomegalovirus

Of the human herpes viruses, CMV is the major cause of morbidity in AIDS patients and is frequently the cause of death.

CMV encephalitis presents as a subacutely progressive diffuse encephalitis evolving over several weeks and characterized by

confusion and imparied sensorium, with variably associated cranial neuropathies, ataxia and motor weakness. Alternatively the presentation may result in focal neurological symptoms corresponding to the location of discrete parenchymal lesions, which may progress to a more diffuse encephalitis. Signs of meningitis may be present. Median survivals following neurological presentation in small series are about a month.

Several recent retrospective studies suggest that polymerase chain reaction amplification technique to detect CMV specific DNA in CSF samples may be a highly sensitive and specific diagnostic test for CMV infection of the CNS.

Necrotizing myelitis attributable to CMV in AIDS presents has been reported by number of authors. Clinical features include paraplegia, urinary retention and hypoesthesia, typical of myelopathy.

CMV polyradiculomyelitis in patients with AIDS presents subacutely with paraesthesias or pain, progressive hypotonic weakness, areflexia and variable sensory deficits ascending from the

lower extremities to involve spinal cord, upper extremities and cranial nerves in some patients.

Neurotuberculosis

Tuberculosis has become an increasingly common problem in HIV – infected persons and extrapulmonary involvement is seen in 60% of cases. In patients with HIV - related tuberculosis positive CSF cultures are obtained in 3% to 10% of the time. Given the difficulty of culturing this organism from CSF, this implies an even higher rate of CNS complication and typically presents as a subacute meningitis. Headache and fever are noted in the majority of cases with encephalopathy, particularly if there is elevated intracranial pressure. Cranial nerve abnormalities and frank meningeal signs are less common. The CSF analysis usually demonstrates a Iymphocytic pleocytosis with a total cell count in the range of 200 to 500/mm^3, hypoglycorrhachia is also commonly observed. Two large series suggest that the clinical presentation, overall CSF profile and prognosis are identical in patients with and without HIV infection. The only difference between seropostive and seronegative patients is an increased incidence of intracerebral mass lesions in the HIV infected group (60% versus 14%).

Isolated CNS tuberculomas may present without concomitant tuberculous meningitis. Their characteristics on cerebral imaging studies have varied; some appears as ring enhancing lesions while others are hypodense and non-enhancing lesions. Anecdotal evidence suggests that CNS tuberculosis may be more common when initial antituberculous therapy has failed, when there is a relapse of disease or when multidrug resistant organisms cause disease. Diagnosis of CNS tuberculosis is still difficult because of the lack of rapid diagnostic tests. Polymerase chain reaction based techniques are used for their purpose. Criteria used for diagnosis of TBM were those previously established by Ogawa et al. A definite diagnosis of TBM was made by isolation of M. tuberculosis from the CSF or the presence of TBM was established by pleocytosis of the CSF and negative bacterial and fungal cultures (including the determination of bacterial antigens and cryptococcal antigen) and at least one of the following 1) a positive tuberculin skin test; 2) evidence of tuberculosis outside the CNS or previous active tuberculosis; 3) CSF glucose levels less than 40mg/dl; and (4) CSF protein levels greater than 0.60g/l.

Nontuberculous mycobacterial CNS infections due to Mycobacterium avium complex and Mycobacterium kansasii have also been described.

Bacterial infections

Pyogenic bacterial infections have been increasingly noted over the course of the HIV epidemic and these infections may precede the onset of severe immuodeficiency. Neurological infection with pyogenic bacteria such us pneumococci and nonpyogenic bacteria like Listeria have been reported though it occurs as a very rare event in HIV patients.

NEOPLASMS

Primary CNS Lymphoma

The first reports of PCNSL in HIV infected patients were published with the initial description of AIDS in 1982. Recently, there has been a dramatic increase in the incidence of PCNSL in association with AIDS. It is estimated that 1% to 2% of all HIV infected patients will develop PCNSL. Epstein Barr virus has been implicated as causative for both systemic and primary CNS lymphoma in association with AIDS or other immunocompromised States. The

prevalence of EBV in AIDS-associated PCNSL has been reported to range between 94% and 100%.

Unlike systemic NHL which can occur at any stage of HIV infection, PCNSL typically occurs in profoundly immunocompromised patients with CD4+ T - Iymphocyte counts below 50cells/mm. Alteration in the level of consciousness and focal neurological deficits are the most common presenting signs of PCNSL. Seizures occur in 23% of AIDS patients with PCNSL while cranial nerve deficits are evident in 13% Signs of increased intracranial pressure are less common. The major difference in presentation between AIDS and non-AIDS related PCNSL are the high prevalence of B symptoms and the shorter duration of symptoms (days to weeks versus months) for patients with HIV related tumors.

Although no radiological finding is pathognomic for PCNSL, some radiological features are suggestive of the diagnosis. A homogenously enhancing lesions in the central gray matter or corpus callosum is highly suggestive of PCNSL. Ring like lesions may occur in 5% to 10% of cases. Most lesions are adjacent to an ependymal or meningeal surface with varying degrees of edema and mass effect. About 50% to 60% of lesions are located peripherally in the

hemispheric gray matter or adjacent white matter. Another 25% of the lesions will be found in the deep midline structures of the septum pallucidum, basal ganglia or corpus callosum.

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.

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. 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, conforming 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.

Seizures

Seizure may be consequence of opportunistic infections, neoplasms or HIV encephalopathy. The seizure threshold lower in these patients owing to frequent electrolyte abnormalities.

Seizure seen in,

Cerebral Toxoplasmosis : 15% to 40%

Primary CNS Lymphoma: 15% to 35%

Cryptococcal Meningitis : 8%

HIV Encephalopathy : 7% to 50%

Seizures also seen in patients with CNS tuberculosis, aseptic meningitis, and progressive multi focal leuco encephalopathy.

In D.M. Holtzman (1997) study, 100 patients with HIV infection presenting with a first seizure, cerebral mass lesion was most common cause, responsible for 32 of the 100 new onset seizure. Of these 32 cases, 28 were due to toxoplasmosis , four lymphoma, HIV encephalopathy associated for an additional 24 new onset seizures. Cryptococcal meningitis was the third most common diagnosis responsible for 13 of the 100 seizures. In 23 cases no cause could be found and these cases represents subcategory of HIV encephalopathy.

MATERIALS AND METHODS

PLACE OF THE STUDY

This study was conducted at the Government Mohan Kumaramangalam Medical College Hospital, Salem. Patients admitted to the wards of the internal medicine and Infectious Disease wards were subjects of the study.

PERIOD OF STUDY

January 2006 to July 2007.

DESIGN

Prospective Randomised cross sectional study.

METHODOLOGY

HIV patients admitted at G.M.K.M.C. Hospital were chosen for the study. Random selection of patients were made in whom a detailed history and clinical evaluation which included the mini mental score (MMSE) was done, after an informed consent from the patient or relative.

The following investigation were done to all patients studied (i.e), when tested positive for HIV.

1. Complete blood count.
2. Renal function test (Sugar, Urea, Creatinine and Electrolytes)
3. Liver Function Test (Bilirubin, AST, ALT, SAP, Albumin)
4. Chest X-ray - P.A View
5. VCTC
6. CD4 count
7. VDRL

All patients with neurological systems were individualised and were subjected to the investigation listed based on clinical findings.

1. C.S.F.
2. CT Brain
3. MRI Brain
4. Creatinine Phosphokinase

METHODOLOGY OF INVESTIGATION

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

CD_4 count was done with Facs Count (Automated Counter).

Tests were done in a single laboratory by the same person, no intrapersonal error was possible.

EXCLUSION CRITERIA

Immuno Compromised state due to any other cause.

LIMITATIONS

- Culture and PCR for mycobacterium could not be done.
- Viral Serology was done only in selected patients.

RESULTS AND OBSERVATIONS

INCIDENCE

31 Patients had neurological manifestations among the 100 Patients studied. The incidence of neurological manifestations in HIV infection, in this study is 31%

SEX DISTRIBUTION

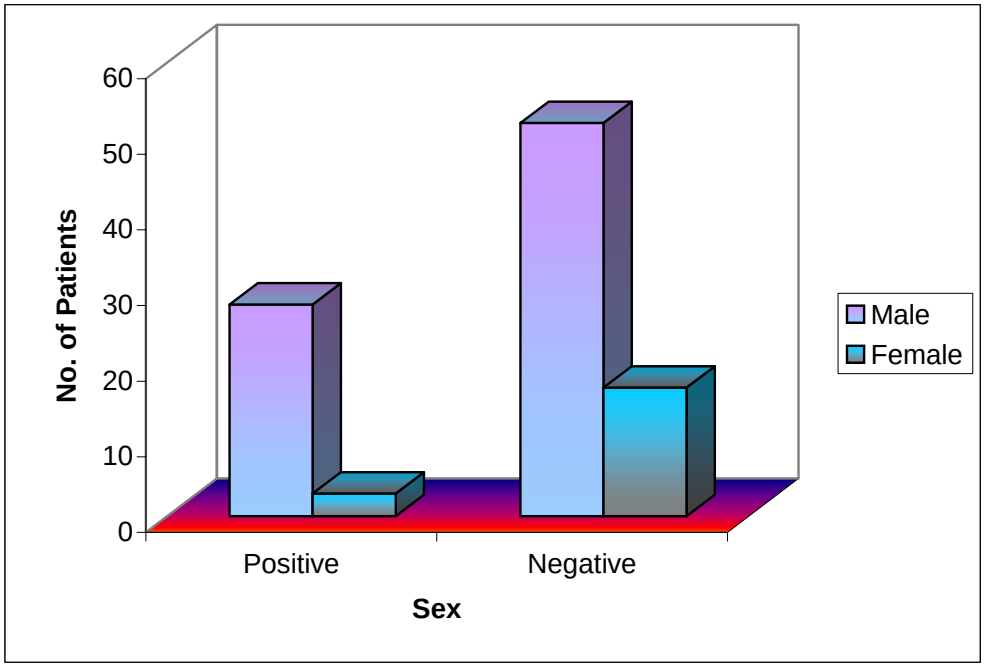
Of the 100 Patients studied 80 were male and 20 were Female. Among the 80 males, 28 had neurological manifestations and of the 20 Females, 3 had neurological Symptoms.

TABLE NO. 1 - shows the sex distribution in this study

Sex	Positive	Negative	Total
Male	28	52	80
	35%	65%	80%
Female	3	17	20
	15%	85%	20%

CHART – 1

SEX DISTRIBUTION



AGE DISTRIBUTION

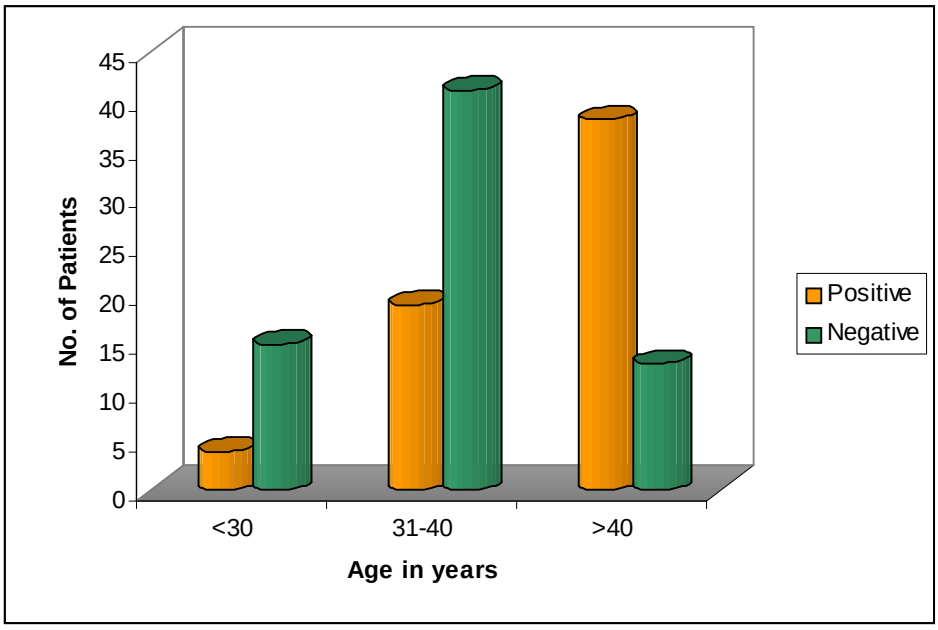
TABLE NO.2 – shows the age distribution in this study

Age in Years	Positive	Negative	Total
<30	4 25%	15 75%	19
31-40	19 31.6%	41 68.3%	60
>40	38 40%	13 62%	21

Majority of the patients in our study were between 31-40 yrs of age. Of the 60 Patients, who were in the age group of 31-40, 19 (31.6%) had neurological symptoms.

CHART – 2

AGE DISTRIBUTION



OCCUPATION

TABLE NO. 3: shows the various occupations involved in this study

Occupation	Positive	Negative	Total
Agriculture	3 33.33%	6 66.66%	9
Daily Labourer	5 23.80%	16 76.19%	21
Driver	14 56%	11 44%	25
House Wife	3 17.64%	14 82.35%	17
Skilled Worker	2 50.008%	2 50.00%	4
Unskilled Worker	4 28.57%	10 71.42%	14
Unemployed	0	4 100%	4
Social Worker	0	1 100%	1
Business	0	4 100%	4
Government Employee	0	1 100	1

In our study most of the patients were drivers (56%) and neurological symptoms were also Common among these group of patients.

MODE OF TRANSMISSION

All Patients in this study group had Hetero Sexual behaviour as the mode of transmission.

TABLE NO. 4

Mode of Transmission	Frequency	Percentage
Hetro Sexual	100	100%
Homo Sexual	-	-

PRE – EXISTING INFECTION

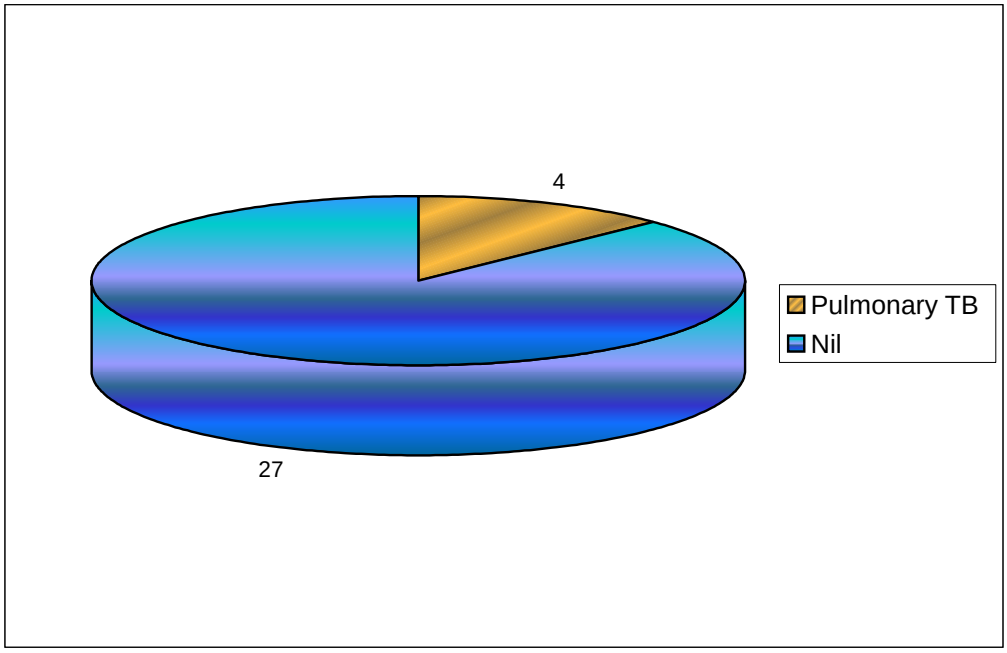
Among 31 Patients who had neurological symptoms, 4 Patient had pulmonary TB as co infection.

TABLE NO.5

Co Infection	Frequency	Percentage
Pulmonary TB (Sputum Negative)	4	12.9%
Nil	27	87.1%

CHART – 3

PRE – EXISTING INFECTION



PHYSICAL ACTIVITY STATUS IN PATIENTS WITH NEUROLOGICAL SYMPTOM

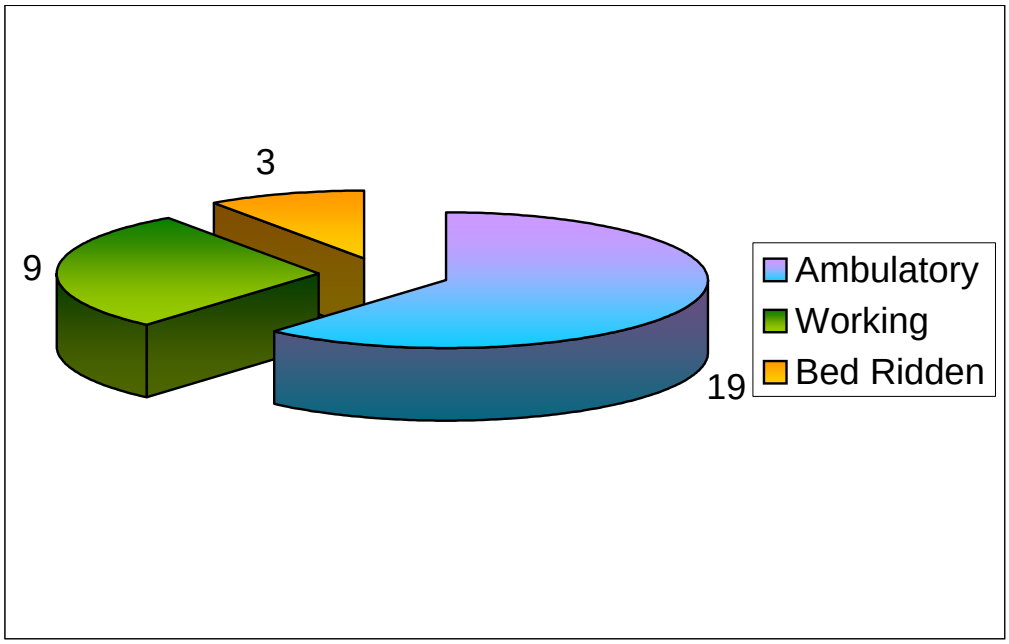
TABLE NO. 6

	Frequency	Percentage
Ambulatory	19	63.33%
Working	9	29.03%
Bed Ridden	3	9.67%

19 Patients in the study group who had neurological manifestation were Ambulatory (i.e. able to do their daily activities but not working), 9 were working and 3 were bed ridden.

CHART – 4

PHYSICAL ACTIVITY STATUS IN PATIENTS WITH NEUROLOGICAL SYMPTOM



CLINICAL PRESENTATIONS

This table shows the various Clinical Presentations and their frequency in the Patients having neurological Manifestations.

TABLE NO. 7

Clinical Presentation	Frequency	Percentage
Headache	22	38.6%
Altered Sensorium	14	24.6%
Hemiplegia	3	5.3%
Seizures	8	14.0%
Paraperesis	4	7.0%
Quradriperesis	2	3.5%
Parasesthesias	2	3.5%
Cerebellar Syndrome	2	3.5%

CHART – 5

ALTERED MENTATION

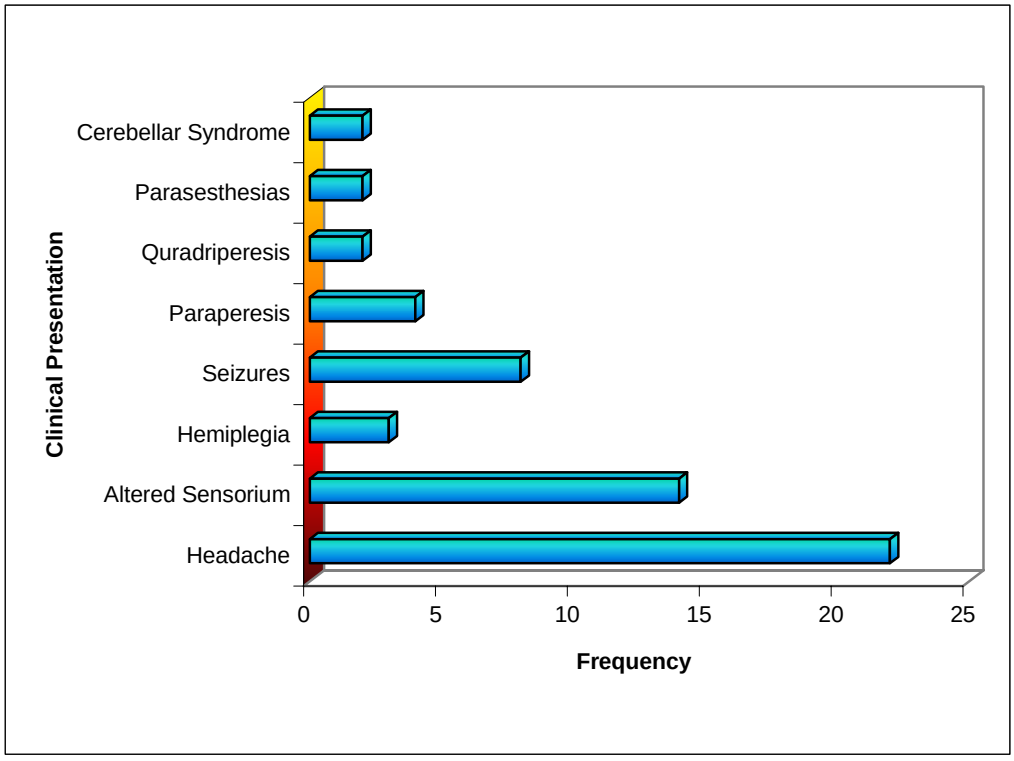


CHART – 6

HEADACHE

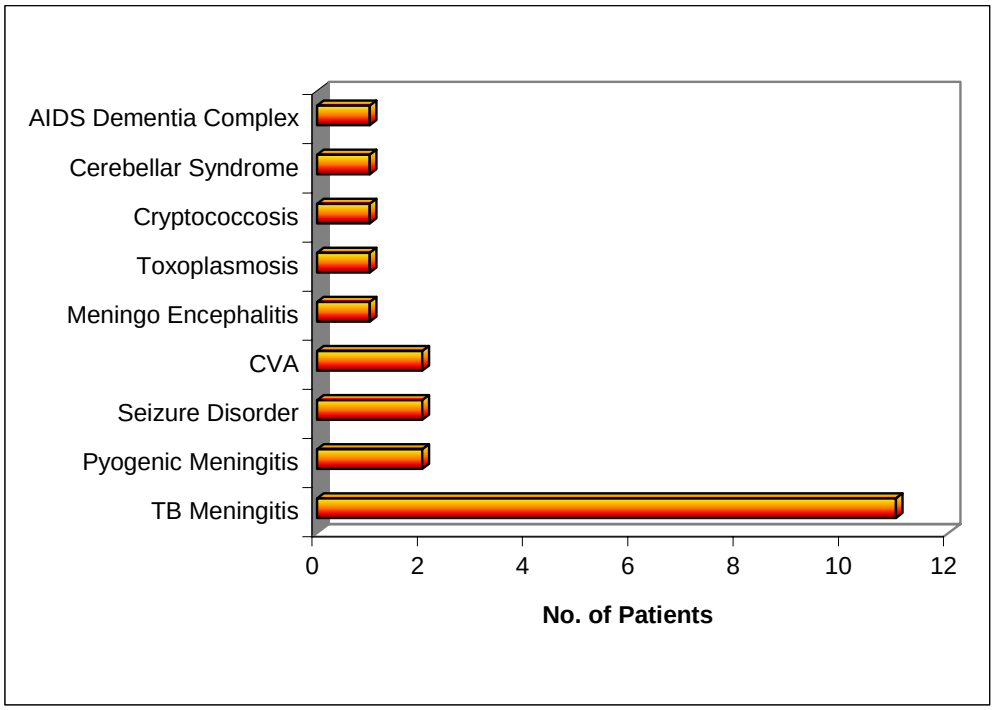


CHART – 7

ALTERED SENSORIUM

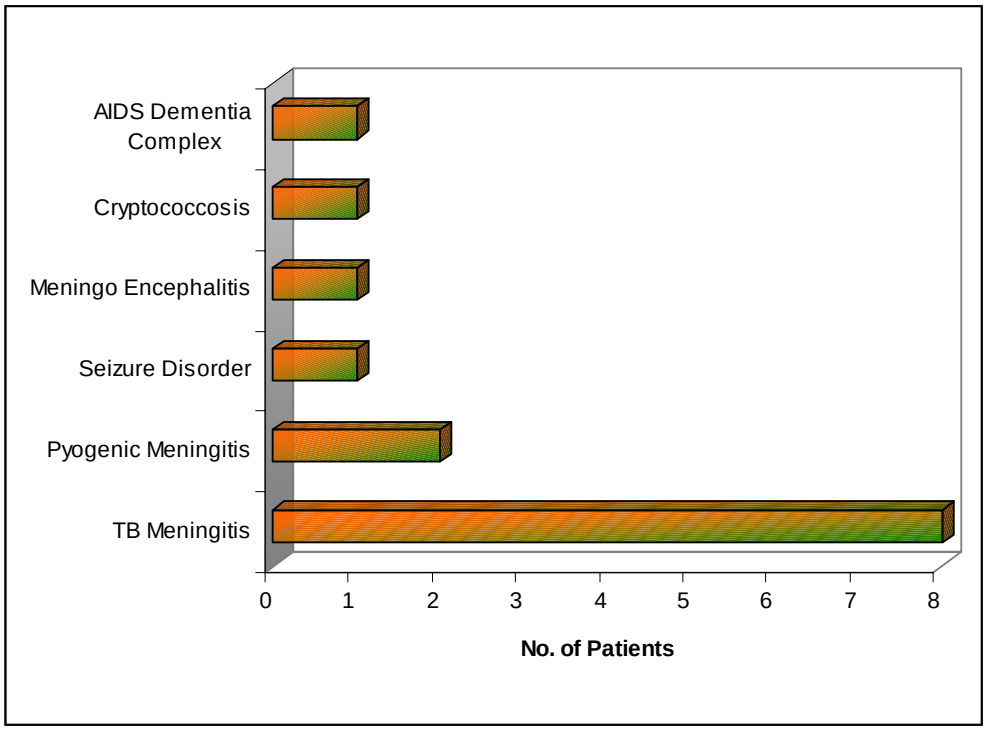
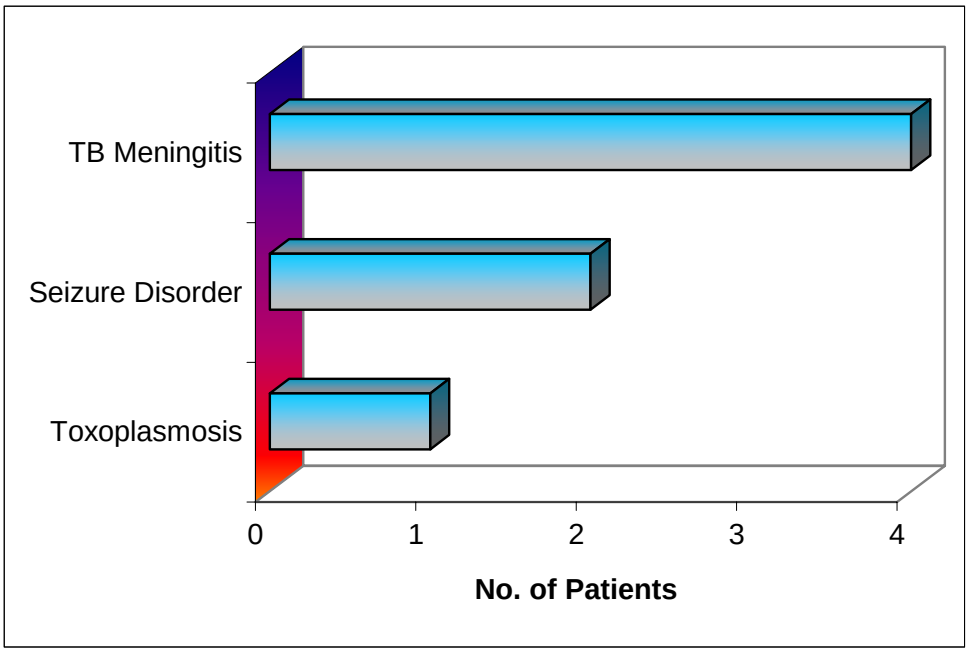


CHART – 8

CONVULSION



DISEASE PATTERN

Shows the disease patterns among patients who had neurological manifestations.

TABLE NO. 8

Diagnosis	Frequency	Percentage
Acute Flaccid Paralysis	1	3.22%
AIDS Dementia Complex	1	3.22%
Cerebellar Syndrome	1	3.22%
Cryptococcal Meningitis	1	3.22%
Toxoplasmosis	1	3.22%
Cerebrovascular Accident	3	9.67%
Guillian Barre Syndrome	1	3.22%
HIV Myelopathv	1	3.22%
Meningoenceephalitis (Cause not determined)	1	3.22%
Multiple Granuloma	1	3.22%
Myopathy	1	3.22%
Peripheral Neuropathy	2	6.44%
Pyogenic Meningitis	2	6.44%
Seizure Disorder	2	6.44%
TB Meningitis	11	35.4%
Tuberculoma	1	3.22%

OUT COME

TABLE NO. 9 : shows the outcome in the study

Out Come	Frequency	Percentage
Improved	20	64.52%
Expired	11	35.48%

11 Patients who had neurological manifestations in the study group expired (35.48%) and 20 Patients had improvement in their clinical condition.

CD_4 COUNT CORRELATION

TABLE NO.10

	CD_4 Count	
	Mean	**SD**
Patient with Neurological Manifestation	179.19	113.16
Patient without neurological Manifestation	225.03	134.58

CD_4 count levels in Patients with neurological manifestations ranged from 11 and 535 with an average of 179.19. The average CD_4 levels in Patients without neurological manifestations was 225.03. There was no statistically significant difference between the two groups. ($P>0.05$)

CD_4 CORRELATION WITH MORTALITY

TABLE NO.11

Out Come	CD_4 Mean	Count SD
Expired	108.38	41.65
Improved	268.60	110.94

The mean CD_4 Count of the patients who expired was 108.38. Mean CD_4 count of the patients and who improved were 231.78 and 268.60. There is a statistically significant correlation of CD4 count among patients who expired (P-0.003**).

CD_4 CORRELATION WITH TB MENINGITIS

There were 10 Patients diagnosed to have TB Meningitis. CD_4 Count for one Patient was not done as the patient died before blood was taken for CD_4 count. The mean CD_4 count of patients with TB Meningitis in the study group was 120.88 and the mean CD_4 count of patients who did not have any neurological manifestations was 225.02. Statistically significant different of CD_4 count was observed between the two groups. (P-0.025*).

TABLE NO.12

	No. of Cases	Mean	SD
Patients with TB Meningitis	11	140.88	43.161
Patients without Neurological Manifestation	69	245.02	138.585

MINI MENTAL SCORE

TABLE NO.13

	MMSE	
	Mean	**SD**
Patient with Neurological Manifestation	24.94	2.13
Patient without neurological Symptoms	26.65	.84

Mini mental Score of Patients with neurological symptoms was compared with those without neurological symptoms. Significant difference was observed in patients with neurological symptoms, P value being less than 0.001.

FUNDUS

Fundus Examination was done for all co-operative patients. 10 patients had features of papilloedema and no patient had features of HIV Retinitis.

CSF ANALYSIS

Analysis was done for 20 patients in the study.

11 Patients had elevated proteins and predominant lymphocytes.

4 Patients had normal CSF.

2 had elevated proteins and acellular smear.

2 patients had predominant neutrophils.

1 had elevated proteins and occasional lymphocytes and also had positivity for cryptococcus in India Ink preparation.

CT BRAIN

24 Patients in the study were subjected to CT Brain among which 3 patients had middle cerebral arterial territory infarct and 1 had multiple calcified granulomata.

MRI

In this study 4 patients had MRI brain done for them. 1 had multiple ring enhancing lesions who was diagnosed to have Tuberculoma and other patients had features suggestive of normal pressure hydrocephalus.

DISCUSSION

In this study, of the 100 seropositive patients, 31 had neurological manifestations (31%). The incidence of neurological manifestations in HIV positive patients according to snider et al was 31% and levy et al was 39%. In India Gupta et al found an incidence of 25.75% in his study.

AGE

Most of the patients in this study were in the age group of 31 - 40 (59.38%). The mean age of the patients with neurological manifestations in a study in university of California and Sanfransisco data was 37.3 years. Mean age in this study was 35.63 years.

SEX

Male patients were found to have neurological manifestations more common (90.63%) as against females (9.38%). Male to female ratio was approximately 9:1. Metha et al, 1999 has reported male predominance with male to female ratio of 12:1.

OCCUPATION

High incidence of neurological manifestations was noted among drivers (56%), followed by daily wages with 23%. 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

All patients with neurological manifestations had heterosexual behaviour as the risk factor. None of our patients had homosexual relationship. Gupta et al found heterosexual relationship in 64.7%, 5.85% in drug abusers and blood transfusion in 14.7%.

PRE-EXISTING INFECTION

Pulmonary Tuberculous was present in four patients with tuberculous meningitis.

CLINICAL PRESENTATION

HEADACHE

This was the commonest presenting symptom in this study. 22 of the 31 patients with neurological symptoms, presented with headache (38.6%). 16 patients (72.72%) had opportunistic infections like tuberculous meningitis, cryptococcosis and pyogenic meningitis as the cause. Six other patients had HIV dementia and multiple granulomata as the cause.

Headache is an extremely common symptom in HIV infection, because of the frequency of intracranial infection and mass lesions. Saag, Gray Bill et al has described headache as a common symptom in HIV infection frequently.

ALTERED SENSORIUM

14 out of the 31 patients, had altered sensorium (24.6%). Altered sensorium as observed in this study was primarily due to a meningeal infection, tuberculous meningitis being most frequent, followed by cryptococcal and pyogenic meningitis. None of the

patients in this study had CNS lymphoma. University of California and Sanfransisco data revealed altered sensorium as a manifestation in secondary viral infection. Progressive multifocal leucoencephalopathy, toxoplasmosis, cryptococcosis, HIV dementia and lymphoma.

SEIZURES

In our study, the common cause for seizures was neurotuberculosis. Of the 31 patients, 8 patients had seizures (14%). Two patients had normal CT brain and C.S.F analysis did not reveal any abnormality. EEG could not be tested to the above patients.

This is perhaps because approximately half the HIV infected patients have no definite identifiable disease of the brain and cerebral HIV infection seems to be the likely cause of the seizures, as reported by Holtzman et al AMJ Med. 1989 study which had HIV encephalopathy as the cause of seizures in 24% of the patients.

PARAPARESIS

4 patients had paraparesis on presentation in our study (7%). Of the 4, one was due Guillian - Barre syndrome and 3 due to HIV myelopathy.

Human T cell lymphotrophic virus 1, tuberculosis, herpes zoster and syphilis were the causes of paraparesis described by A.I Bhigjee et al in their study.

PARAESTHESIAS

Two patients in our study had paraesthesias of both lower limb (3.5%). One patient was on antiretroviral therapy (which included zidovudine) and other patient was not on ART. Both were improved with amitryptilline and nutritional support.

Fuller, Le Fauchur et al (2001) has shown an incidence of 9.46% of peripheral neuropathy in his study.

CEREBELLAR SYNDROME

Of the 31 patients 1 had features of cerebellar syndrome (3.22%). One patient had an hypodense lesion in the cerebellar area in the CT brain (plain).

Mc Arthur et al (1998) had noticed gait disturbance and clumsiness in 45% of patients with HIV dementia.

Comparative Table : **1**

	Vijay D. Teja et al	**This study**
Number of Patients	100	100
Incidence	32 %	31%
Headache	13 (40.63%)	22 (38.6%)
Altered sensorium	14 (20.6%)	14(21.6%)
Hemiplegia	4 (12.5%)	3(5.3%)
Seizures	8(25.07%)	8 (14.0%)
Paraparesis	6 (18.75%)	4(7.0%)
Paraesthesias	3 (9.35%)	2(3.5%)
Cerebellar Syndrome	3 (9.35%)	2 (3.5%)
Involuntary Movements	1 (3.13%)	--
Psychosis	3 (9.35%)	--

AIDS DEMENTIA COMPLEX

Among the 31 patients, one had AIDS dementia complex (3.22%). Patient presented with headache and progressive cognitive decline. Mini mental score of the patient was 20. CT brain and C.S.F analysis were normal.

Impaired memory and concentration with psychomotor slowing represent the common early presentation of this disorder.

Vijay D. Teja et al (2005) reported 8.03% incidence in their studies. 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

In our study two patients had peripheral neuropathy (6.44%). Both the patients presented with paraesthesias and were foot drop. One was taking antiretroviral therapy which included zidovudine and other not on antiretroviral.

HIV associated sensory neuropathies include both distal sensory polyneuropathy due to HIV infection and antiretroviral toxicity. It is very difficult to differentiate between the two. Treatment is largely symptomatic. Our patients improved with change of retro viral regimen, amitryptilline and nutritional support.

MYOPATHY

One patient in our study had myopathy (3.22%). The patient presented with myalgia, proximal muscle weakness. On investigating further he had elevated creatinine kinase levels. Patient was on

antiretroviral therapy. After stopping zidovudine patient was followed up, with improvement in symptoms.

Studies have suggested that zidovudine induced myopathy occurs only when an underlying HIV related inflammatory myopathy is present.

HIV MYELOPATHY

Of the 31 patients in the study, two had HIV related myelopathy (6.44%). Patient had lower limb weakness and urinary incontinence on presentation. MRI spine showed no abnormalities and C.S.F analysis was normal.

Jerez.p et al (2001) have shown 22% incidence of spinal lesions in AIDS. Leading cause of myelopathies described in association with HIV was vacuolar myelopathy followed by myelitis.

NEUROTUBERCULOSIS

12 out of 31 patients who had neurological symptoms in our study had tuberculous infection of the nervous system. Among the 12 patients, 11 had tuberculous meningitis (35.4%) and 1 had

tuberculoma (3.22%). 3 of the 11 patients with tuberculous meningitis expired (27.27%).

The patient diagnosed with tuberculoma presented with headache and partial seizures involving left upper limb. MRI brain revealed multiple ring enhancing lesions. C.S.F analysis showed elevated protein with predominant lymphocytes.

Increased number of neurotuberculosis in Indian studies is probably due to the high prevalence of tuberculosis in this part of the world.

In all our patients tuberculous meningitis was the first manifestation of the disease. Among them five patients on Antiretroviral therapy.

PYOGENIC MENINGITIS

2 patients had features of pyogenic meningitis (6.44%). Both the patients presennted with altered sensorium, fever and headache. CT brain was normal and C.S.F analysis revealed elevated proteins

and predominant neutrophils in cytology. C.S.F culture did not grow any organism.

Both the patients however succumbed to the disease proving the point that pyogenic infection coexisting with HIV infection has very high mortality.

AIDS related CNS complication from bacterial pathogens have not been reported from western studies.

Studies from NIMHANS – S.K. SANKAR, ANITHA MAHADEVAN et al (2005) show 9% incidence of Bacterial meningitis.

CRYPTOCOCCAL MENINGITIS

Of the 31 patients one had cryptococcal meningitis (3.22%). Headache, altered sensorium and signs of meningeal irritation was the presentation. C.S.F analysis in this patient was positive for Cryptococcus on India ink preparation.

Bandypadhyay et al in his study had 3.7% incidence of cryptococcal meningitis.

TOXOPLASMOSIS

Of 31 patients one had toxoplasmosis (3.22%). Head ache and fever was the presentation. IgG Ab positive for Toxoplasmosis and MRI was normal.

SINGH et al in his studies shows 3.6% incidence of Toxoplasmosis.

CEREBROVASCULAR ACCIDENT

3 patients in our study presented with cerebrovascular complications (9.66%). All three patients presented with hemiparesis and their CT brain showed middle cerebral arterial territory infarct. On admission and he expired on the same day. Evaluation of the 3 patients for young stroke showed no abnormalities.

Gupta et al has reported 8.82% incidence of CVA in seropositive patients in his study.

There is a broad spectrum of etiologies causing this scenario but in many cases the pathogenesis is unclear. Cerebral granulomatous angitis due to HIV infection could result in vascular occlusive disease.

GUILLIAN-BARRE SYNDROME

Among the 31 patients with nerological symptoms, 1 had Guillian – Barre syndrome (3.22%). Both the patients presented with features of ascending paralysis. C.S.F analysis showed elevated protein with acellular smear cytology. Nerve conduction study and Oligoclonal band in C.S.F could not be done.

HIV–GBS occurs in early and late stages of HIV infection, and may follow onset of AIDS. TH Brannagan et al had reviewed 10 patients with HIV–GBS between 1986 and 1999, in which GBS was first symptom of the HIV infection in 3 patients.

SEIZURE DISORDERS

Two patients in this study group presented as seizure disorder (6.44%). One patient presented with generalized seizure. CT brain and C.S.F analysis were normal in both the patients. EEG could not be done.

Approximately half of HIV infected patients with seizures have no definite identifiable disease of the brain and cerebral HIV infection seems to be the most likely cause of the seizures. It the study by Holtzman et al, HIV encephalopathy was responsible for seizures in 24% of the patients.

MULTIPLE GRANULOMATA

In our study one patient presented with chronic headache of 6 months duration. CT brain done on the patient showed multiple calcified granulomas. C.S.F analysis revealed no abnormality. As the patient could not afford MRI brain was not done. Patient was empirically treated with albendazole with no apparent improvement on immediate follow up.

MORTALITY

20 out of the 31 patients who had improved outcome (35.48%).

As improved Antiretroviral Therapy, nutritional and social support continues to the prolong life span of HIV infected persons.

Comparative Table: **2**

	Gupta et al	**Vijay D. Teja et al**	**Our study**
Year of Study	1993	2005	2007
Incidence	25.75%	32%	31%
Mode of transmission	Heterosexual - 64.5% I.V Drug abuser - 5.85 % Blood transfusion - 14.7 %	Heterosexual –100%	Heterosexual - 100%
AIDS dementia complex	17.65%	3.13%	3.22%
Peripheral neuropathy	8.82%	6.25%	3.5%
Neurotuberculosis	58.82%	31.25%	35.4%
Cryptococcal meningitis	8.8%	3.13%	3.22%
Neurosyphilis	--	3.13%	--
PML	--	3.13%	--
Myopathy	--	3.13%	3.22%
Toxoplasmosis	3.8%	--	3.22%
CVA	8.82%	9.38%	9.67%
Seizure disorder	--	6.25%	6.44%
Outcome	--	Poor	Good

CONCLUSION

1. Incidence of neurological illness in HIV infection in our study was 31%.

2. All patients in our study had heterosexual transmission of disease.

3. CNS manifestations in men were more common than in women.

4. Headache and altered mentation were the two common symptoms observed in this study.

5. Tuberculous meningitis was the most commonest opportunistic infection in our study.

6. No significant CD4 count correlation was found between the patients with neurological manifestations and those without neurological manifestations.

7. CD4 count when less was associated with increased mortality.

8. Patients with coexisting tuberculous meningitis and HIV infection had significantly lower CD4 counts.

9. Tuberculous meningitis was associated with good outcome and pyogenic meningitis had high mortality.

10. Patients with neurological manifestations had good outcome and low mortality.

SUMMARY

We study 100 consecutive HIV sero positive patients from January 2006 to July 2007 of them 31 had neurological manifestations. Out of which TB meningitis constituted major part.

The following were the details of neurological manifestations. Tuberculous meningitis(35.4%), cerebrovascular complications (9.67%), Guillian barre syndrome (3.22%), pyogenic meningitis (6.44%), peripheral neuropathy (6.44%), seizure disorders (6.44%), acute flaccid paralysis (3.22%), AIDS dementia complex (3.22%), cerebellar syndrome (3.22%), cryptococcal meningitis (3.22%), Toxoplasmosis (3.22%), HIV myelopathy (3.22%), meningoencephalitis - cause not determined (3.22%), multiple granulomata (3.22%), myopathy (3.22%), Tuberculoma (3.22%).

Mortality increased most with coexisting meningitis and with decreased CD4 counts.

Commonest neurological condition associated was neurotuberculosis.

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PROFORMA

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 : Lymph nodes:

Oral Cadidiasis :

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

DC

ESR

Urine Routine

LFT

RFT

Serum Electrolytes

Blood Sugar

Chest X-Ray

Sputum Examination

CEREBROSPINAL FLUID STUDY:

Cell – Count

Type

Proteins

Sugar

Staining

Culture

Others

SPECIAL INVESTIGATIONS:

FINAL DIAGNOSIS:

COURSE IN THE HOSPITAL:

MASTER CHART

S. No.	Name	Age	Sex	Occ	Mot	Clinical Presentation	CT	MMSE	CSF	CT	MRI	Diagnosis	Outcome
1	Moorthy	28	M	DL	HS		120	27					
2	Gunabalan	40	M	Agri.	HS	Headache, Stiffneck	114	26	↑ L, Pr.	Normal	-	TBM	Good
3	Mohan	39	M	Driver	HS		186	26					
4	Thangavelu	47	M	DL	HS		206	26					
5	Sekar	49	M	Driver	HS		536	27					
6	Santha	36	F	HW	HS	Convulsion, AS	168	28	Normal	Normal		SD	Good
7	Karuppannan	36	M	DL	HS	Lt. Foot drop	180	28				PN	Good
8	Arthanari	35	M	Driver	HS		226	28					
9	Sangeetha	24	F	HW	HS		214	25					
10	Munusamy	40	M	Agri.	HS	AS, Headache	80	-	↑ Pr, No.	Normal		PM	Expired
11	Chelladurai	40	M	DL	HS		288	27					
12	Perumal	42	M	DL	HS		94	-					
13	Revathi	32	F	HW	HS		529	24					
14	Kumari	36	F	HW	HS		50	-					
15	Selvarani	40	F	HW	HS		178	-					

16	Natarajan	45	M	Driver	HS	Headache, AS	254	25		Normal		TBM	Good
17	Vanitha	23	F	HW	HS		286	24					
18	Vijaya	28	F	HW	HS		222	26					
19	Madhu	46	M	Driver	HS		136	26					
20	Sivakumar	46	M	DL	HS		177	28					
21	Solomon	38	M	DL	HS		168	24					
22	Dharman	41	M	DL	HS		190	27					
23	Murugesan	30	M	Driver	HS		366	27					
24	Vairavel	40	M	DL	HS		30	27					
25	Santhakumar	30	M	DL	HS		50	27					
26	Kaviarasu	31	M	Driver	HS	Headache, AS	80	24	↑ L, Pr.	Normal		TBM	Good
27	Santhanam	30	M	Driver	HS	Weakness of Limbs (UL & LL)	136	27	↑ Pr.	Normal		AFP	Expired
28	Kaliyamurthy	36	M	DL	HS		164	26					
29	Rajamani	30	M	DL	HS		225	26					
30	Ansari	35	M	SW	HS		236	28					
31	Jeyaraj	29	M	DL	HS	Foot Drop	330	28	Normal			PN	Good
32	Rajan Babu	31	M	Driver	HS		364	27					

33	Kumaravelu	29	M	DL	HS		408	26					
34	Palanisamy	42	M	Agri.	HS		480	26					
35	Subrathinam	33	M	DL	HS		540	26					
36	Selvakumar	32	M	Driver	HS	AS, Headache	89	-	↑ Pr.	Normal		PM	Expired
37	Raja	40	M	DL	HS	Headache, Convulsion	124	27	↑ L, Pr.	Normal		TBM	Good
38	Anbarasu	39	M	DL	HS		176	23					
39	Indrabalan	43	M	DL	HS		212	26					
40	Deepak Lal	41	M	DL	HS		264	27					
41	Chenniappan	39	M	UE	HS	AS & SN	344	-	↑ No.	Normal	Normal	ME	Expired
42	Velraj	29	M	Driver	HS		365	27					
43	Kasiraj	33	M	UE	HS		412	27					
44	Semaraj	31	M	Business	HS	V, Headache, SN	65	-	↑ Pr. G Normal	Normal		Toxo	Expired
45	Irusappan	29	M	Agri.	HS	Convulsion	142	-	↑ L, Pr.	Normal		TBM	Good
46	Jeyakumar	42	M	Business	HS		171	28					
47	Prabu	47	M	DL	HS		213	22					
48	Riyaz	31	M	Driver	HS	Weakness of Limbs (UL & LL)	289	27		Infarct MCA (T)		CVA Rt. HP	Expired
49	Kalaiselvi	32	F	HW	HS		325	28					

50	Sivakumar	33	M	Govt.E.	HS	Weakness of Limbs (UL & LL)	376	28	Normal	Normal	Normal	HIV, Myelopathy	Good
51	Kamal Hussain	29	M	UE	HS		513	22					
52	Anand	36	M	SW	HS	AS & Headache	94		Indianink +ve	Normal		Crypto	Expired
53	Ebinezer	39	M	Driver	HS		125	27					
54	Selvan	41	M	DL	HS		177	28					
55	Madhan	47	M	UE	HS		220	24					
56	Saravanan	33	M	UE	HS	Convulsion	253	26		Multiple Gr lesion		Multiple Granuloma	Good
57	Palanivel	53	M	Driver	HS		324	27					
58	Muthu	40	M	UE	HS	AS	91		↑ L, Pr.	Normal		TBM	Expired
59	Arumugam	60	M	UE	HS		114	23					
60	Nagarajan	37	M	NE	HS		200	28					
61	Seetha	29	F	HW	HS	Headache, Fever	206	27	↑ L, Pr.	Normal		TBM	Good
62	Muniyan	32	M	Agri.	HS	Weakness of Limbs (UL & LL)	291	27		Rt. MCA infarct		CVA. Lt. HP	Expired
63	Maharaja	34	M	Driver	HS		54	28					
64	Jone	36	M	Business	HS	Headache, Fever	136	26	↑ L, Pr.			TBM	Good
65	Rajaya	43	M	Driver	HS	Weakness of Limbs (UL & LL)	128	27	↑ Pr.		Normal	GBS	Expired
66	Ganesan	37	M	Agri.	HS	Weakness of Limbs (UL & LL)	98	24		Lt. MCA infarct		CVA Rt. HP	Good

67	Devendran	39	M	Driver	HS		77	22					
68	Chellaiyan	40	M	Driver	HS	Unsteadiness	102	26		Hypodense Lt.	Normal	Cerebellar Syndrome	Good
69	Palanisamy	31	M	Agri.	HS		54	27					
70	Chinnupaiyan	35	M	Agri.	HS		194	28					
71	Singaravelu	50	M	Business	HS		206	26					
72	Selvi	26	F	HW	HS		176	27					
73	Chinnayyan	36	M	Driver	HS	Headache, V, Fever	209	27	↑ L, Pr.	Normal		TBM	Good
74	Periyasamy	40	M	Driver	HS		189	27					
75	Kalakumari	34	F	HW	HS		236	26					
76	Vijaya	20	F	HW	HS		111	24					
77	Veeramuthu	33	M	Agri.	HS		178	26					
78	Raji	21	F	DL	HS		210	27					
79	Madanlal	37	M	DL	HS		285	28					
80	Kumari	24	F	HW	HS		134	28					
81	Rathinaselvi	29	F	HW	HS		176	-					
82	Hamitha Begam	42	F	HW	HS		286	28					
83	Valli	33	F	HW	HS	Convulsion	324	28		Normal	Normal	Seizure Decoder	Good

84	Jeyapal	23	M	Driver	HS	Headache & AS	101	22	↑ L, Pr.	Normal		TBM	Good
85	Rajaselvan	56	M	Driver	HS	AS	161	-	Normal	Normal		ADC	Expired
86	Sankar	39	M	So.W	HS		215	27					
87	Anbuselvi	33	F	HW	HS		257	27					
88	Muthu	35	M	UE	HS	Headache, Convulsion	116	22		Normal	Ringleision	Tuberculoma	Good
89	Jeyapriya	37	F	HW	HS		173	27					
90	Jegatheesan	53	M	So.W	HS		210						
91	Raja	49	M	Un.SW	HS	Weakness, PX of muscle	251	26				Myopathy	Good
92	Helen	59	F	HW	HS		283	28					
93	Krishnan	33	M	Driver	HS		326	27					
94	Ramasamy	53	M	Driver	HS		116	24					
95	Dhanasekaran	46	M	Un.SW	HS		173	27					
96	Murugesan	43	M	UE	HS		210	27					
97	Joseph	40	M	DL	HS		253	27					
98	Kalanjiyam	43	M	DL	HS		254	26					
99	Prabakaran	50	M	DL	HS	AS	126	23	↑ L, Pr.	Normal		TBM	Good
100	Sekar	39	M	DL	HS		191	-					

MOT - Mode of Transmission

Occ - Occupation

MMSE - Minimental Score Examination

CT - Computer Tomography

MRI - Magnetic Resonance

DL - Daily Labour

Agri. - Agriculture

HW - House Wife

SW - Skilled Worker

UE - Unemployed

NE - Not Employed

Govt. E - Govt. Employed

So.W - Social Worker

Un.SW - Unskilled Worker

HS - Hetro Sexual

AS - Altered Sensorium

UL & LL - Upper Limb and Lower Limb

V - Vomitting

PX - Proximal

L - Lymphocyte

Pr - Protein

G - Glucose

No. - Neutrophil

MCA - Middle Cerebral Atery

HP - Hemiparesis

TBM - Tuberculosis Meningits

PN - Peripheral Neuropathy

SD - Seizure Disorder

PM - Pyogenic Menengitis

AFP - Acute Flaccid Paralysis

Toxo - Toxoplasmosis

ME - Meningo-Encephalitis

Crypto - Cryptococcocis

GBS - Gullian - Barre Syndrome

ADC - AIDS Dementia Complex