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A Study of Peripheral Neuropathy in HIV Infected Patients

Submitted in partial fulfillment of the requirements towards the conferment of

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DEPARTMENT OF NEUROLOGY

TIRUNELVELI MEDICAL COLLEGE

TIRUNELVELI

CERTIFICATE

This is to certify that this dissertation entitled **'A study of Peripheral Neuropathy in HIV infected patients'** submitted by **Dr.K.Gunasekaran** appearing for D.M., Degree examination in August 2010 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the The Tamil Nadu Dr.M.G.R. Medical University, Chennai.

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DECLARATION

I Dr. K.Gunasekaran do solemnly affirm that this dissertation titled "A study of Peripheral Neuropathy in HIV infected patients" is done by me at Department of Neurology, Tirunelveli Medical College & Hospital, Tirunelveli, during the year 2009 under the guidance and supervision of Dr.B.Sritharan, M.D.,D.M., Professor and Head, Department of Neurology, Tirunelveli Medical College.

The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of D.M., degree in Neurology.

Place: Tirunelveli

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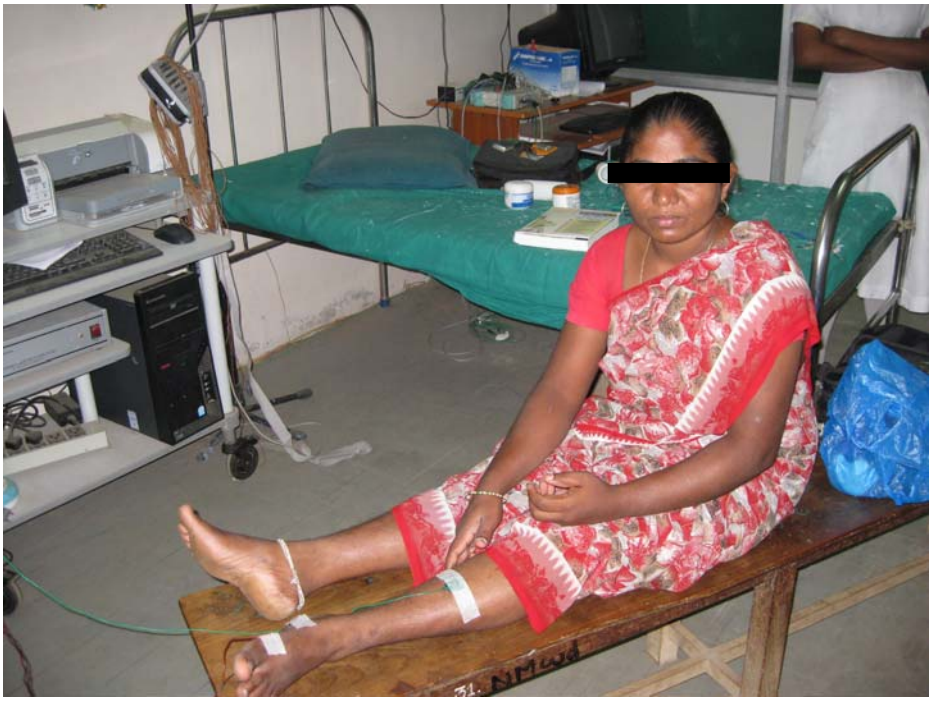

Patient undergoing Electrophysiological study

Introduction

The life expectancy of HIV-infected patients has increased as a result of highly active antiretroviral therapy (HAART). Consequently, patients and physicians are dealing with neurologic complications from the HIV disease, from concurrent diseases, and from drugs used to treat it. Peripheral neuropathy is the most common HIV-associated neurologic complication. The spectrum and the frequency of this complication are changing due to introduction of new antiretroviral drugs, an aging HIV-infected population, and the emergence of other long-term complications of HIV and/or its treatment.Several forms of neuropathy may occur, depending on the level of immunosuppression and the presence of risk factors. There is a great need for an improved understanding of these complications and their pathogenetic mechanisms, for the development of effective therapies that provide adequate symptomatic relief and halt or reverse the damage to the nerves. This work of dissertation has been done with an aim of estimating the prevalence and evaluating the risk factors associated with peripheral neuropathy in HIV infected patients of our region.

Aims of the study

1. To study the prevalence of peripheral neuropathy in HIV infected patients.

2. To study the risk factors associated with the development of peripheral neuropathy in HIV infected patients

3. To study the clinical profile and various types and patterns of peripheral neuropathy in HIV infected patients.

Review of Literature

EPIDEMIOLOGY

Human immunodeficiency virus (HIV) is a lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome (AIDS), a condition in human in which the immune system begins to fail, leading to life-threatening opportunistic infections. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells. The four major routes of transmission are unsafe sex, contaminated needles, breast milk, and transmission from an infected mother to her baby at birth (vertical transmission).

HIV infection in humans is considered pandemic by the World Health Organization (WHO). From its discovery in 1981 to 2006, AIDS killed more than 25 million people. HIV infects about 0.6% of the world's population.[3] In 2005 alone, AIDS claimed an estimated 2.4–3.3 million lives, of which more than 570,000 were children. Antiretroviral treatment reduces both the mortality and the morbidity of HIV infection.

HIV infects primarily vital cells in the human immune system such as helper T cells (to be specific, CD4+ T cells), macrophages, and dendritic cells. HIV infection leads to low levels of CD4+ T cells through three main mechanisms: First, direct viral killing of infected cells; second, increased rates of apoptosis in infected cells; and third, killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4+ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections.

HIV-1 causes most HIV infections worldwide, but HIV-2 causes a substantial proportion of infections in parts of West Africa. HIV-2 appears less virulent than HIV-1.

Most untreated people infected with HIV-1 eventually develop AIDS. These individuals mostly die from opportunistic infections or malignancies associated with the progressive failure of the immune system.[4] HIV progresses to AIDS at a variable rate affected by viral, host, and environmental factors; Most will progress to AIDS within 10 years of HIV infection: some will have progressed much sooner, and some will take much longer. Treatment with anti-retrovirals increases the life expectancy of people infected with HIV. Even after HIV has progressed to diagnosable AIDS, the average survival time with antiretroviral therapy was estimated to be more than 5 years as of 2005.[5] Without antiretroviral therapy, someone who has AIDS typically dies within a year.[6]

STAGING

HIV disease staging and classification systems are critical tools for tracking and monitoring the HIV epidemic and clinical management. Two major classification systems currently are in use: the U.S. Centers for Disease Control and Prevention (CDC) classification system and the World Health Organization (WHO) Clinical Staging and Disease Classification System.

The CDC disease staging system assesses the severity of HIV disease by CD4 cell counts and by the presence of specific HIV-related conditions. The definition of AIDS includes all HIV-infected individuals with CD4 counts of <200 cells/μL (or CD4 percentage <14%) as well as those with certain HIV-related conditions and symptoms. The CDC system is used in clinical and epidemiologic research.

In contrast to the CDC system, the WHO Clinical Staging and Disease Classification System (revised in 2005) can be used readily in resource-constrained settings without access to CD4 cell count measurements or other diagnostic and laboratory testing methods. The WHO system classifies HIV disease on the basis of

clinical manifestations that can be recognized and treated by clinicians in diverse settings, including resource-constrained settings, and by clinicians with varying levels of HIV expertise and training.

CDC Classification System for HIV Infection

The CDC categorization of HIV/AIDS is based on the lowest documented CD4 cell count (Table 1) and on previously diagnosed HIV-related conditions (Tables 2 and 3). For example, if a patient had a condition that once met the criteria for Category B but now is asymptomatic, the patient would remain in Category B. Additionally, categorization is based on specific conditions, as indicated below. Patients in categories A3, B3, and C1-C3 are considered to have AIDS.

Table 1. CDC Classification System for HIV-Infected Adults and Adolescents

	Clinical Categories		
CD4 Cell Categories	A Asymptomatic, Acute HIV, or PGL (persistant generalised lymphadenopathy)	B Symptomatic Conditions, not A or C	C AIDS-Indicator Conditions
(1) ≥500 cells/μL	A1	B1	C1
(2) 200-499 cells/μL	A2	B2	C2
(3) <200 cells/μL	A3	B3	C3

Table 2. CDC Classification System: Category B Symptomatic Conditions

Category B symptomatic conditions are defined as symptomatic conditions occurring in an HIV-infected adolescent or adult those meet at least 1 of the following criteria:

a) They are attributed to HIV infection or indicate a defect in cell-mediated immunity.
b) They are considered to have a clinical course or management that is complicated by HIV infection.

Examples include, but are not limited to, the following:

- Bacillary angiomatosis
- Oropharyngeal candidiasis (thrush)
- Vulvovaginal candidiasis, persistent or resistant
- Pelvic inflammatory disease (PID)
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Hairy leukoplakia, oral
- Idiopathic thrombocytopenic purpura
- Constitutional symptoms, such as fever (>38.5°C) or diarrhea lasting >1 month
- Peripheral neuropathy
- Herpes zoster (shingles), involving ≥2 episodes or ≥1 dermatome

Table 3. CDC Classification System: Category C AIDS-Indicator Conditions

- Bacterial pneumonia, recurrent (≥2 episodes in 12 months)
- Candidiasis of the bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical carcinoma, invasive, confirmed by biopsy
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1-month duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcers (>1-month duration), or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1-month duration)
- Kaposi sarcoma
- Lymphoma, Burkitt, immunoblastic, or primary central nervous system
- Mycobacterium avium complex (MAC) or M kansasii , disseminated or extrapulmonary
- Mycobacterium tuberculosis , pulmonary or extrapulmonary
- Mycobacterium , other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis jiroveci (formerly carinii) pneumonia (PCP)
- Progressive multifocal leukoencephalopathy (PML)
- Salmonella septicemia, recurrent (nontyphoid)
- Toxoplasmosis of brain
- Wasting syndrome due to HIV (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhea (≥2 loose stools per day ≥1 month) or chronic weakness and documented fever ≥1 month

WHO Clinical Staging of HIV/AIDS and Case Definition

- The clinical staging and case definition of HIV for resource-constrained settings were developed by the WHO in 1990 and revised in 2007. For the purpose of the WHO staging system, adolescents and adults are defined as individuals aged ≥15 years.

Clinical Stage I:

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage II:

- Moderate unexplained* weight loss (under 10% of presumed or measured body weight)**
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular chelitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical Stage III:

- Unexplained* severe weight loss (over 10% of presumed or measured body weight)**
- Unexplained* chronic diarrhoea for longer than one month
- Unexplained* persistent fever (intermittent or constant for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia

- Pulmonary tuberculosis
- Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained* anaemia (below 8 g/dl), neutropenia (below 0.5 billion/l) and/or chronic thrombocytopenia (below 50 billion/l)

Clinical Stage IV:

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Recurrent septicaemia (including non-typhoidal Salmonella)

- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

Footnotes:

- * Unexplained refers to where the condition is not explained by other conditions.
- ** Assessment of body weight among pregnant woman needs to consider the expected weight gain of pregnancy.

NEUROLOGICAL COMPLICATIONS OF HIV

In the early 1980s, as the systemic manifestations of the acquired immunodeficiency syndrome (AIDS) were first described, investigators realized that human immunodeficiency virus (HIV) infection could affect the nervous system at every level [7]. The spectrum of neurological disorders is broad and involves the central nervous system, or CNS (brain and spinal cord) and the peripheral nervous system, or PNS (nerves outside the brain and spinal cord, and related muscle).

The causes of neurological disease are various: autoimmune reactions due to immune disregulation, opportunistic infections (OIs), metabolic and nutritional derangement due to or associated with AIDS, the direct attack on nerve tissue by HIV, and the toxic effects of drugs used to treat HIV and OIs.

PERIPHERAL NEUROPATHY IN HIV INFECTION

Although every part of the neuraxis with the exception of the neuromuscular junction is susceptible to HIV infection, the peripheral nervous system is one of the frequent targets and the most common neurologic problem. The major form of peripheral neuropathy in HIV disease is distal symmetric polyneuropathy (DSP) [57]. Several other

peripheral neuropathy types [59] are associated with HIV disease, mainly acute and chronic inflammatory demyelinating polyradiculoneuropathies (Guillain-Barre-like diseases), mononeuropathy multiplex (MM), progressive polyradiculopathy (PP), and autonomic neuropathy (AN).

Distal Symmetric Polyneuropathy

Distal symmetric polyneuropathy affects over one third of patients with AIDS [8]. It is rarely seen in children and is most common in the late stages of HIV disease. HAART (Highly Active Anti Retroviral Therapy) lessens disease progression, improves immunity, and significantly lowers risk of developing distal symmetric polyneuropathy.

The clinical symptoms of distal symmetric polyneuropathy are numbness, burning, and tingling sensations in the feet, usually in a symmetric pattern; paresthesias or aching distally in the lower extremities; and hyperesthesia (e.g., contact sensitivity, such as with bed sheets or socks). In late stages of distal symmetric polyneuropathy, the upper extremities may also be affected, although to a milder degree.

The exam consists first of "subjective" sensory testing, where the examiner uses, 128 Hz tuning fork, a safety pin and cotton swabs to assess vibration, thermal, pain and light touch sensation. It is important to check all four modalities. Next, the "objective" portion of the exam consists of checking the reflex pattern and muscle bulk and strength. In distal symmetric polyneuropathy, one would expect a diminution or loss of the ankle jerk reflexes.

While depressed or absent ankle reflexes relative to the knees, is a hallmark of distal symmetric polyneuropathy, it is important to note that as HIV disease progresses, distal symmetric polyneuropathy is often combined with central nervous system disease, such as dementia or myelopathy. In this case, reflex testing may reveal hyperactive or brisk knee reflexes with normal ankle reflexes. Other clinical features of distal symmetric

polyneuropathy include increased vibratory thresholds and reduced pinprick and temperature sensation in a stocking and glove distribution. Muscle strength and joint position sensation are relatively normal. Symptomatic weakness appears late in the disease and is generally restricted to the distal intrinsic foot muscles. Another objective sign of distal symmetric polyneuropathy is atrophic skin change, particularly a significant loss of hair from the distal extremities. Nerve conduction studies can be useful to confirm the diagnosis of distal symmetric polyneuropathy by revealing abnormal sensory nerve potential amplitudes and conduction velocity, especially of the sural nerve.

Other Causes of distal symmetric polyneuropathy: It is critical to differentiate HIV-related distal symmetric polyneuropathy from distal symmetric polyneuropathy resulting from other causes, such as diabetes mellitus, vitamin B_{12} deficiency, alcohol abuse, or drug toxicities (e.g., vincristine, used to treat Kaposi's sarcoma and lymphoma; isoniazid and thalidomide, used to treat aphthous ulcers).

Differentiating HIV-Related Distal Symmetric Polyneuropathy from Neurotoxic Neuropathy

The major antiretroviral neurotoxins [11] are the dideoxynucleoside analogues didanosine (ddI), zalcitabine (ddC), and stavudine (d4T). Other forms of NRTIs (3TC [Epivir], AZT [Retrovir], and abacavir [Ziagen], along with non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors, are not generally associated with peripheral neuropathy.

Hydroxyurea, a drug used to treat cancer that may also help certain anti-HIV drugs work better, appears to increase the risk of peripheral neuropathy. Other drugs used in the treatment of HIV-related disorders that can increase the chance of developing peripheral neuropathy include:

- Isoniazid, (INH), used to treat tuberculosis
- Metronidazole, used to treat amoebic dysentery
- Vincristine, used for Kaposi's sarcoma and non-Hodgkin's lymphoma
- Thalidomide, used to treat cancers and severe mouth ulcers
- Ethambutol, used to treat Mycobacterium avium complex (MAC)

The clinical features of nucleoside-related distal symmetric polyneuropathy and distal symmetric polyneuropathy resulting from primary HIV infection are so similar as to be virtually indistinguishable on bedside examination. Simpson et al. reported that the prevalence of HIV-associated neuropathy increases as immune function deteriorates. [9] This relationship suggests that a patient presenting with high CD4 counts may not be suffering from HIV-associated distal symmetric polyneuropathy alone, but also from neurotoxicity or other underlying conditions.

In neurotoxic distal symmetric polyneuropathy, the standard time to resolution of neuropathy after discontinuation of the neurotoxin is at least eight weeks. Many patients improve within one to three weeks following discontinuation of zalcitabine but resolution of distal symmetric polyneuropathy may also take considerably longer. Patients taking higher doses of zalcitabine (e.g., 0.06 mg/kg/ day) experience a "coasting period" of three to six months following withdrawal of the drug, during which time the symptoms of neuropathy may intensify before improving. [10] A maximum didanosine dosage of 12.5 mg/ kg/day has been suggested to avoid the development of distal symmetric polyneuropathy. Immunosuppressed patients with low CD4 cell counts may develop didanosine- associated neuropathy at lower doses. [9]

Pathology and pathophysiology of Distal Symmetric Polyneuropathy

Length-dependent axonal degeneration of sensory fibers, with little evidence of nerve-fiber regeneration, characterizes distal-sensory polyneuropathy. Both large myelinated and unmyelinated nerve fibers are lost. The overt neuropathological changes include inflammatory infiltrates of lymphocytes and activated macrophages, low numbers of dorsal-root ganglion neurons, and high numbers of nodules of Nageotte. [12]. The envelope glycoprotein, gp120, may produce neurotoxicity within the dorsal root ganglion. The prominent presence of proinflammatory cytokines, including tumor necrosis factor, interferon, interleukin 6, and other inflammatory mediators including nitric oxide, has been shown in dorsal root ganglia.

Little is known about the specific pathological changes of antiretroviral-toxic neuropathy, although sural-nerve biopsies have shown severe axonal destruction, prominent in unmyelinated fibers. Prominent mitochondrial abnormalities have also been shown, and are thought to underlie the pathogenesis of antiretroviral-toxic neuropathy. This is further supported by evidence of increased serum lactate concentrations and reduced serum concentrations of acetylcarnitine in patients with antiretroviral-toxic neuropathy. Dideoxynucleoside inhibition of neurite outgrowth is dose-dependent. The mechanism of neuronal injury from zalcitabine and other neurotoxic drugs seems to be distinct from the neurotoxicity of the envelope glycoprotein, gp120. Thus, zalcitabine mediates injury through neuronal necrosis, whereas gp120 is predominantly apoptotic and mediated through Schwann cells.

Treatment of Distal Symmetric Polyneuropathy

The treatment of HIV-associated distal symmetric polyneuropathy is primarily symptomatic. Correction of metabolic and nutritional abnormalities. Pain management begins with nonopioid analgesics, such as acetaminophen and nonsteroidal anti-inflammatory agents. With persistent and more disabling pain, adjuvant agents such as

tricyclic antidepressants may be added. Amitriptyline to be started at 10 to 25 mg at bedtime and increased by 25 mg increments on a weekly basis to a maximum of 100 to 150 mg. Side effects include anticholinergic toxicity and if these side effects persist and limit dose escalation, a tricyclic antidepressant with a lower anticholinergic profile may be used (e.g., nortriptyline or desipramine). Anticonvulsants such as phenytoin, carbamazepine, gabapentin and lamotrigine may also provide relief from pain.

Plasmapheresis has been ineffective in reducing symptoms of Distal Symmetric Polyneuropathy. Topical capsaicin may reduce the pain of Distal Symmetric Polyneuropathy. When increasing levels of disabling pain are refractory to the above-mentioned agents, a strong opioid or long-lasting opioid agonist (e.g., methadone or long-acting morphine or fentanyl) may be considered.

Inflammatory Demyelinating Polyneuropathy

Inflammatory demyelinating polyneuropathy is a relatively infrequent neuropathic complication of HIV infection seen most often in patients who are HIV seropositive but otherwise asymptomatic. The acute form (AIDP) may occur at the time of primary HIV infection. AIDP is clinically characterized by rapidly progressive muscle weakness involving two or more extremities, accompanied by generalized areflexia. Bilateral peripheral facial nerve weakness may be present. The chronic form (CIDP) is clinically distinguished by its slower progression; its clinical course may be monophasic or relapsing. Cerebrospinal fluid analysis is important in the diagnosis of HIV-associated inflammatory demyelinating polyneuropathy. The majority of HIV-infected patients have a CSF lymphocytic pleocytosis (10 to 50 cells/mm^3), with mild elevation of protein. This finding serves to distinguish them from HIV-negative inflammatory demyelinating polyneuropathy patients, whose CSF is typically acellular. [13] Electrophysiologic studies

reveal evidence of demyelination in patients with inflammatory demyelinating polyneuropathy.

Inflammatory demyelinating polyneuropathy is primarily treated by immunomodulation (corticosteroids, plasmapheresis, and high-dose intravenous immunoglobulin). In severely compromised patients (CD4 count less than 50 cells/mm^3), anti-cytomegalovirus (CMV) therapy with ganciclovir, foscarnet, or cidofovir, singly or in combination, is warranted.

Mononeuritis Multiplex

Mononeuritis multiplex is a rare complication that occurs in either early or late stages. [14] When mononeuritis multiplex occurs early, it is often the result of a self-limited dysimmune neuropathy or vasculitis. In patients with long-standing HIV-1 infection and CD4 cell counts less than 50/μL, an association with cytomegalovirus (CMV) infection has frequently been noted. Mononeuritis multiplex has also been associated with varicella zoster [15] and hepatitis C infections [54]. Multifocal sensory and motor abnormalities in the distribution of cutaneous nerves, mixed nerves, and nerve roots, including cranial neuropathies, constitute the typical neurologic presentation of MM. MM associated with CD4 counts greater than 200 cells/mm^3 generally has a limited distribution and is characterized by the acute onset of sensory or motor deficits limited to one or a few peripheral or cranial nerves [16]. These deficits usually resolve spontaneously or within several months of receiving immunomodulating therapy. Patients with advanced immunodepression develop an extensive and more rapidly progressive form of MM, which may simulate other peripheral neuropathies, such as inflammatory demyelinating polyneuropathy or progressive polyradiculopathy. The diagnosis of mononeuritis multiplex is supported by electrophysiologic examination that

reveals a multifocal pattern of reduction in evoked sensory and motor compound muscle action potential amplitudes.

Progressive Polyradiculopathy

Progressive polyradiculopathy is an uncommon but well-described complication of HIV infection. The incidence is thought to have declined in the era of HAART. It is usually attributed to CMV infection [17]. However, it can be caused by other conditions, including lymphoma, [18] syphilis, [19] mycobacterial infections, [20] herpes simplex virus,[21]and cryptococcus [22]

Progressive polyradiculopathy usually occurs in patients with advanced HIV disease and in patients with low CD4 cell counts. The onset is subacute, and the course extends for days to weeks. The earliest symptoms are low back pain with radiation into one leg followed by progressive leg weakness. If not promptly identified and treated, the symptoms rapidly progress to a flaccid paraplegia with bowel and bladder incontinence. Upper extremities may be involved late in the course [17]. Polymerase chain reaction amplification of CMV DNA in CSF is sensitive tool

The major electrophysiologic abnormalities seen are widespread denervation in paraspinal muscles, reflecting axonal loss in lumbosacral roots with later denervation potentials in the leg muscles. Nerve conduction study results are usually normal. Although it may show enhancement of lumbosacral meninges and nerve roots, the main utility of magnetic resonance imaging is to exclude focal mass lesions that may be compressing the cauda equina. Pathologic features include marked inflammation and necrosis of the dorsal and ventral nerve roots with cytomegalic inclusions detectable in endothelial cells and nerve parenchyma.

Current choices for the treatment of CMV disease are ganciclovir, foscarnet, and cidofovir. Treatment of HIV-associated progressive polyradiculopathy attributable to

other causes is directed at the specific cause (eg, anti-mycobacterials for tuberculosis, intravenous penicillin for syphilis, and chemotherapy for lymphoma-related disease).

Autonomic Neuropathy

Failure of the sympathetic autonomic nervous system is manifested by orthostatic hypotension, syncope, diarrhea, and anhidrosis. Parasympathetic abnormalities include resting tachycardia, impotence, and urinary dysfunction [23]. A variety of factors may contribute to the clinical manifestations of autonomic dysfunction, including malnutrition, dehydration, central and peripheral nervous system abnormalities, and drugs used to treat HIV-associated complications, such as tricyclic antidepressants, vincristine, and pentamidine.

Diffuse infiltrative Lymphocytosis Syndrome (DILS) [58]

Persistent CD8 lymphocytosis, named diffuse infiltrative lymphocytosis syndrome is characterized by a persistent peripheral blood polyclonal CD8 lymphocytosis and by visceral CD8 T-cell infiltration, including salivary glands, lungs, kidneys, gastrointestinal tract, and peripheral nerves[24]. Clinically, diffuse infiltrative lymphocytosis syndrome presents as acute or subacute painful multifocal, most often symmetrical, neuropathy. Electrophysiologic studies show axonal neuropathy. Nerve biopsy specimens are characterized by marked angiocentric CD8 infiltrates and abundant expression of HIV p24 protein without vessel wall necrosis. The treatment of diffuse infiltrative lymphocytosis syndrome consists primarily of standard antiretroviral therapy and/or corticosteroids.

Vasculitis

Virtually every pattern of vasculitis of small, medium, and large vessels has been encountered in HIV-1 infection [25] but it is a rare event, occurring in 0.3% to 1.0% of patients with AIDS. Vasculitis of the peripheral nerve can occur either as an isolated

process or, more commonly, as a manifestation of a systemic disease [26]. Vasculitic damage in the peripheral nervous system may present with clinical features of Distal Symmetric Polyneuropathy. Peripheral nerve examination shows variable loss of myelinated axons and ongoing axonal degeneration with focal distribution in different fascicles. Perivascular inflammatory cell infiltration and fibrinoid necrosis of small epineural blood vessels are observed. Vasculitis is treated with corticosteroids or intravenous immunoglobulin.

EVALUATION OF PERIPHERAL NERVE DISEASES

VARIOUS PATTERNS OF PERIPHERAL NEUROPATHY

Several patterns of peripheral nerve involvement are recognized. The prototypic and most common pattern is length-dependent, with sensory loss and pain preceding distal weakness. As progressively shorter nerves are affected, symptoms and signs unroll as a stocking up the leg. The nerve length at the knee level approximately equals the length innervating the hand, and with further progression, symptoms and signs unroll as a long glove up the arm. The distribution is usually symmetric. In. the extreme, a shield loss over the chest and abdomen can be observed when nerve length involvement reaches the circumference of the thorax. As a corollary, it is rare in polyneuropathy for there to be sensory involvement to the waist level, especially without marked sensory loss also to the elbows. Accordingly, isolated sensory loss to the upper thigh and waist levels suggests central nervous system localization (myelopathy). When the pattern of symptoms and signs includes both proximal and distal limb involvement, the pathologic process is usually demyelination at multifocal sites along roots and nerves (inflammatory polyradiculoneuropathy). Acute and chronic forms occur (AIDP and CIDP).

Table: Patterns of Peripheral Neuropathy and Examples of Disorders and Causes

1.	Sensory-motor symmetric(length dependent pattern)	Diabetes, medications, toxins, metabolic disorders, hereditary
2.	Sensory-motor symmetric (proximal and distal pattern)	Acute inflammatory demyelinating polyradiculopathy, chronic inflammatory demyelinating polyradiculopathy
3.	Sensory-motor asymmetric(nerve or plexus pattern)	Diabetic amyotrophy, idiopathic plexopathy, vasculitic mononeuritis multiplex
4.	Sensory-motor asymmetric	Porphyria, leprosy
5.	Sensory symmetric or asymmetric	Paraneoplastic neuronopathy, Sjogren syndrome, idiopathic ganglionitis, vitamin B6 toxicity, leprosy
6.	Motor symmetric or asymmetric	Amyotrophic lateral sclerosis, multifocal motor conduction block neuropathy, lower motor neuron syndrome, Poliomyelitis
7.	Autonomic symmetric or asymmetric	With other neuropathies (diabetes, acute inflammatory demyelinating polyradiculopathy), isolated involvement (amyloidosis)

TIME COURSE

An acute onset is defined as days to several weeks. Most chronic neuropathies are steadily progressive. A history of clear remissions and exacerbations suggests CIDP or other form of immune-mediated neuropathy. When the time course clearly starts in adult

life, an acquired neuropathy is more likely than a hereditary disorder. When the time course cannot be dated, a hereditary neuropathy should be considered.

1.	Acute	Apoplectic	Vasculitic mononeuritis multiplex, idiopathic plexopathy
		Days to weeks	Acute inflammatory demyelinating Polyradiculopathy, porphyria, acute toxic exposure, proximal diabetic neuropathy, paraneoplastic sensory neuropathy
2.	Chronic	Years	Diabetic Polyneuropathy Chronic inflammatory demyelinating polyradiculopathy,idiopathic
		Insidious	Hereditary

TYPES OF NERVE FIBER INVOLVEMENT

The peripheral nervous system can be divided into somatic and autonomic components, and somatic peripheral nerves can be further divided into sensory and motor functions. Within the somatic nervous system, sensory and motor fiber involvement can be accurately assessed and there are neuropathies affecting sensory, motor, or both types of fibers. In the autonomic nervous system, separating sensory (afferent) from motor (efferent) involvement is difficult and both are commonly affected. Neuropathies with isolated autonomic nervous system involvement are rare.

SYMPTOMS

From the chief complaint it may not be apparent which types of nerves are involved. Nerve dysfunction can be expressed as negative and positive Symptoms. Positive symptoms are felt to reflect inappropriate spontaneous nerve activity detected by the patient as uncomfortable and painful sensations, or other spontaneous phenomena. Negative symptoms reflect loss of nerve signaling. An important clinical difference between sensory and motor somatic nerves involves compensatory mechanisms. Following motor nerve loss, surviving motor nerves undergo collateral reinnervation to

reinnervate orphaned muscle fibers. This compensatory process has the effect of blunting weakness due to mild motor nerve loss, and clinical weakness may not be apparent to the patient or on physical examination until 50% of motor nerve fibers are lost (80% in slowly progressive denervating disorders) [27]. However, positive symptoms of cramps and fasciculations may be present early on as the only clinical indication of motor nerve involvement. The needle EMG is sensitive in detecting early motor fiber loss and will confirm motor nerve involvement.

Other Important Histories in Peripheral Neuropathies

Medical History

Past and current medical histories like diabetes mellitus, certain collagen vascular disorders, chronic renal failure, and HIV infection. Inquiring about medication use is important, and should include vitamins and other over the counter compounds. Although the list of drugs, compounds, and vitamins associated with peripheral neuropathies is limited, drug-induced neuropathies represent readily treatable causes.

Family History

An important line of inquiry is the family history, seeking evidence to support a hereditary neuropathy. Although it may seem that a hereditary condition should be known within a family, the slow progression and variable expression masks detection. Interestingly, in large families with known Charcot-Marie-Tooth neuropathy, <30% of affected individuals seek medical attention for their symptoms [30]. Therefore, a careful line of questions can be very informative when there are clinical features suggesting a very long-standing condition, such as insidious onset, high arches, and hammertoes.

SIGNS

The clinical neurologic examination is sensitive for peripheral nerve loss and dysfunction, and informative for localization. It is important to emphasize that the sensory

examination can be challenging and confusing because responses are indirect and represent a patient's interpretation of the testing questions. For example, does the sensory loss follow a stocking-glove (distal predominate), dermatomal, or radicular pattern? The sensory examination frequently focuses on determining whether there is "large fiber" or "small fiber" involvement, based on a battery of simple clinical tests. However, psychophysical sensory perception testing suggests these distinctions are more apparent than real because of overlap between nociception, touch, and_pressure stimulus properties. Although nociceptive information is conveyed by small diameter nerve fibers, some nociceptive receptors are innervated by myelinated fibers, and subjects can distinguish sharp from dull stimuli without feeling pain. Formal psychophysical testing of nociception is performed using hot stimuli, cold stimuli, and special equipment, which contrasts to clinical sensory testing performed using cool instruments (tuning fork and reflex hammer) and sharp objects of varying shape (safety pin, broken wooden stick. and commercial pin probe). Cutaneous mechanoreceptors are mainly innervated by large diameter nerve fibres and are activated by a variety of moving stimuli. Vibratory thresholds are suitable indicators of large diameter sensory nerve dysfunction.

Table: Positive and Negative Symptoms Associated With Nerve Damage

			Positive symptoms	**Negative symptoms**
1	Somatic nerves	Sensory	Pain, tingling	Numbness, lack of feeling
		Motor	Cramps, fasciculations	Weakness, atrophy
2	Autonomic nerves		Hyperhydrosis, diarrhea	Orthostatichypotension,impotence anhydrosis,constipation

Touch Stimuli

Application of the lightest touch to the dorsum of the hand and foot represents a measure of low threshold mechanoreception. A series of monofilaments can be applied to

grade the severity of touch loss. Ten-gram filaments are useful because lack of touch perception at this level of pressure is associated with risk for unappreciated trauma.

Vibration Stimuli

Tuning forks of 128 Hz assess larger diameter nerve fiber function. Various comparisons can be made, and it is very important that patients are fully attentive and understand the need to indicate complete disappearance of the vibration. Comparisons between patient and examiner for the disappearance of the vibration can be measured in seconds. Alternatively, the time for the vibration to disappear for the patient after the tuning is forcefully struck can be measured in seconds. Empiric data from the great toe indicate that young adults lose vibration perception after 15 s, with a loss of 1 s per decade of age, and a loss of vibratory perception in < 10 s is abnormal at any age.

Sharp Stimuli

The goal is to apply a sharp stimulus without also applying undo pressure on the skin. A distinction between noxious and light pressure stimuli can be made by gently applying the two ends of a safety pin in association with a three-part question: “which is sharper, the first application, the second application, or are both the same?”. Inability to distinguish between sharp and dull supports loss of nociceptive fibers relative to low-threshold mechanoreceptor fibers.

Position Sense

The ability to detect changes in digital joint position is normally exquisite (two degrees). It is important that patients understand the degree of sensitivity requested, and that they are blinded to the testing. Accordingly, misperception of joint movements (including falsely perceived position changes), and insensitivity to movements are significant for loss of large-diameter fibers. Profound joint position loss is unusual in peripheral nerve disorders, and often reflects central nervous system involvement.

Deep Tendon Reflexes

Tendon reflexes represent an objective measure sensory nerve function. The myotatic reflex consists of a monosynaptic arc with large-diameter afferent (sensory) nerve fiber input from muscle spindle fibers and large-diameter efferent (motor) nerve fiber output from alpha motor neuron fibers. The reflex is much more vulnerable to sensory nerve fiber than to motor nerve fiber damage. Accordingly, an absent reflex is an objective indication of significant dysfunction of large-diameter sensory fibers. However, assurance that the reflex is truly absent is essential, and reinforcing maneuvers, such as clinching the jaw or fists and the Jendrassic maneuver, should be used before the reflex is considered absent. Tendon reflexes diminish with age, and although precise data are not available, an absent Achilles reflex after the age of 80 years may be normal.

Table: NINDS Scale for Deep tendon Reflexes [28]

Grade	Reflex response
0	Reflex absent
1	Reflex small, less than normal: includes trace response, or response brought out only with reinforcement
2	Reflex in lower half of normal range
3	Reflex in upper half of normal range
4	Reflex enhanced, more than normal: includes clonus

Motor Signs

Detecting motor nerve involvement can be challenging due to the compensatory process of collateral innervation that obscures early effects of denervation. Muscle inspection for atrophy is useful, and the extensor digitorum brevis muscle will show the early change in the feet and first dorsal interosseous muscles early changes in the hands. A certain degree of age-related motor fiber loss occurs above 65 years and must be taken into consideration. Inspection for contraction fasciculations is useful to detect motor fiber

loss. Contraction fasciculations are visible twitches of a muscle during early activation, and represent the discharge of individual motor units. Such twitches are not visible in muscles with normal numbers of motor units, but enlarged motor units from denervation and collateral reinnervation are readily observed.

Strength testing can be optimized to detect mild degrees of weakness by assessing muscles that can be just overcome on manual muscle testing in normal individuals. Informative muscles in the legs include flexors and extensors of the lesser toes and the extensor of the great toe, and in the arms include abductors of the second and the fifth digits and extensors of the fingers. Ankle dorsiflexion weakness occurs in more severe neuropathies, but ankle plantar flexion weakness is evident only in the most severe neuropathies [29]. Subtle weakness of ankle dorsiflexion and plantar flexion can be tested best during gait assessment by having patients walk on their heels and toes or hop on one leg at a time.

Autonomic System Signs

The autonomic nervous system is involved in many peripheral neuropathies, but symptoms and signs of dysautonomia are uncommonly voiced by the patient and must queried. Orthostatic dizziness and changes in blood pressure (a drop of >30 mmHg systolic pressure and >15 mmHg diastolic pressure recorded 60—90 s after standing support autonomic involvement. Impotence has many causes, but is frequently associated with autonomic neuropathy. The sicca symptoms (dry eyes and mouth) are associated with the Sjogren syndrome and represent end organ failure of salivary and tear glands. Sjogren syndrome is associated with sensory neuropathies.

Bony Changes

Limb inspection should include structural changes in the lower legs, feet and hands. The following changes may be encountered in normal individuals, but in the

setting of a peripheral neuropathy evaluation, suggest a long-standing condition. The angle between the shin and the unsupported foot is normally about 130°, and a larger angle suggests weakness of ankle dorsiflexor muscles, High arches and hammertoe deformities suggest long standing differences in the muscular forces exerted on the bones of the foot leading to foreshorten feet. Fallen arches can also be observed in severe neuropathies. Toe and foot injuries unnoticed by the patient suggest a marked degree of sensory loss. In the hands, flexion contractions of the fingers suggest weakness of finger extensor muscles. Inability to adduct the fifth digits suggests weakness of lumbrical muscles.

Other Signs

Mild dependent pedal edema, rubor, coolness and shininess of the lower leg and foot despite good distal arterial pulses, suggests decreased movements of distal leg muscles caused by mild muscle weakness, reducing the vascular return of blood and lymph.

PATHOLOGICAL CHANGES

Determining the primary pathologic process is important for diagnosis, treatment, and prognosis. The two basic pathologic processes are demyelination and axonal loss. They may occur together, especially when the primary process is demyelination because demyelination frequently involves immune attack and axons can be damaged as innocent bystanders.

Electrodiagnostic testing is most able to distinguish axonal from demyelinating primary pathology. Nerve biopsy is less practical and informative in this regard for several reasons. Biopsies evaluate only a small segment of sensory nerves, and the relevant pathologic process may be missed. Biopsies are rarely repeated, and the time course of changes cannot be followed. A nerve biopsy leaves permanent dysfunction, and most biopsies are of sensory nerves because a localized area of numbness is tolerable

whereas permanent weakness is not. Nerve biopsy is important when vasculitis is a consideration and a biopsy can detect rare causes of neuropathy due to deposition of protein or other substance, such as amyloid, and abnormal cells such as sarcoid (granulomas) and malignant cells.

ELECTRODIAGNOSTIC EVALUATION OF PERIPHERAL NEUROPATHY

Questions that can be answered with electrodiagnostic testing include the following:

(i) Which elements are involved (sensory nerves, motor nerves, or both)?

(ii) What is the underlying pathology (primary demyelination, primary axonal, or mixture)?

(iii) What is the distribution of nerve damage (single nerve, multiple nerves, length-dependent pattern, plexus, roots, symmetric, or asymmetric)? And (iv) What is the time course (ongoing or chronic)?

TECHNICAL ISSUES

Temperature is the most important controlled variable. Limbs should be warm, with temperatures above 31°C. If cool, limbs should be thoroughly warmed with an external heat source. Supramaximal nerve stimulation must be obtained (defined as 120% of the current required to achieve a maximal response) to ensure a maximal nerve response, but over- stimulation should be avoided because it may lead to activation of adjacent nerves. Attention to placement of stimulation electrodes over the appropriate nerve results in lower currents to achieve maximal responses. Identification of anomalous innervation in the forearm (Martin—Gruber) is essential because it can mimic ulnar nerve conduction block in the forearm.

Determination of the motor point cannot be made from anatomical landmarks and requires trial and error placements to determine which site yields the largest CMAP

amplitude [31]. Similar concerns apply to placement of recording electrodes for sensory nerve action potentials (SNAP) [32].

STATISTICAL ISSUES:

Nerve Conduction - Limits of Normal

Nerve conduction values are delimited by statistically derived limits of normal, determined from data obtained from "normal" subjects. Common limits used in nerve conduction studies are; (i) lower limits of normal for sensory and motor response amplitudes and Conduction velocities and (ii) upper limits of normal for distal latencies and F- and H-wave latencies. These limits vary somewhat between laboratories, and commonly represent 2—3 standard deviations from normally distributed data or 95% confidence limits from asymmetrical data. Erroneous classifications can easily occur. For example, patient height (limb length) is an important variable that influences distal latency, F-wave latency, and conduction velocity values, and should be incorporated in limits of normal for these values [33].

Conduction velocity values vary 3—5 m/s and F-wave latencies vary 6—8 ms over the common height range of 60 in. to 72 in. [33]. Reporting values as "normal' or "abnormal" may he misleading, and the degree of the abnormality should he considered. A related issue is values just above or below the normal limits may not be the expected value for that individual. Thus, in a patient with normal extensor digitorum muscle bulk and strength, a CMAP value just at the lower limits of normal more likely represents suboptimal placement of the recording electrode than pathology because the expected value for a normal subject should be close to the mean value in the distribution. Similarly, in a young diabetic patient, a peroneal motor conduction velocity just above the lower limits of normal more likely reflects pathologically slowed conduction rather than normal conduction because the expected velocity should be close to the mean value

Collateral Reinnervation

Collateral reinnervation is a compensatory process whereby surviving motor nerve terminals reinnervate denervated muscle fibers. The effect is to preserve both muscle strength and CMAP amplitude until further loss of motor nerve fibers exceeds the capacity of reinnervation to keep up, leading to fall of strength and CMAP amplitude. As a consequence of collateral reinnervation, CMAP amplitude values may remain above the lower limit of normal until 50—80% or more of axons have degenerated, depending on the rate of denervation. Mild degrees of axonal loss occur with normal aging >65 years, affecting the lowere limit of normal among the very elderly. Needle EMG is the most sensitive indicator of previous and active axonal loss.

Symmetry of Nerve Conduction Values

The peripheral nervous system can reasonably be considered symmetric, with the expectation that corresponding nerve conduction results from the right and left sides will be of similar value. Practical aspects of nerve conduction studies can lead to some degree of asymmetry of values. Asymmetric limb temperatures can affect side-to-side measures of amplitude distal latency and conduction velocity. Suboptimal placement of recording electrodes can give false asymmetric CMAP amplitude values [34].

Table: Limits of Asymmetry in Normal Nerve Conduction Studies

	Motor nerves				Sensory nerves		
	Median	Ulnar	Peroneal	Tibial	Median	Ulnar	Sural
Amplitude	0.5	0.7	0.2	0.4	0.6	0.5	0.4
Distal latency	1.3	1.3	1.4	1.4	1.2	1.2	1.2
Conduction velocity	0.8	0.9	0.8	0.8	0.8	0.8	0.8
F-wave latency	1.1	1.1	1.1	1.1			

Needle EMG Sampling

Needle EMG can answer two basic questions: (i) Is there evidence for denervation? (ii) What is the nature of the denervation? Evidence for denervation is the presence of abnormal spontaneous activity in the form of positive sharp waves and fibrillation potentials. These potentials are very sensitive for motor nerve damage, but cannot distinguish between pathologic causes (neuropathic vs. myopathic). Distinguishing among pathologic causes can be determined by assessment of motor unit action potentials (MUAPs) recorded at low levels of voluntary muscle activation. Despite these restrictions, it is possible to distinguish neuropathic MUAPs from myopathic MUAPs by their recruitment pattern and by assessment of their waveforms.

NERVE CONDUCTION STUDIES

Normal Nerve Conduction

A whole nerve consists of hundreds of myelinated axons whose diameters range from 7 to 12 m. Nerve conduction studies are typically preformed by percutaneous electrical stimulation of all axons in a nerve and recording the resultant evoked response. Sensory and motor nerves can be studied separately by varying the placement of the recording electrodes. The conduction velocity of a nerve fiber is proportional to its axon diameter, leading to a range of nerve fiber conduction velocities. Within a nerve, 35-70 m/s for sensory nerves and 35-55 m/s for motor nerves [35]. For sensory nerves, recording electrodes are placed over the nerve, and the evoked response (SNAP) represents the summed activity of all sensory nerve fiber action potentials. For motor nerves, recording electrodes are placed over the muscle and the evoked response (CMAP) represents the summed activity of all muscle fiber action potentials. Accordingly, the CMAP includes synaptic delays across neuromuscular junctions. Following nerve stimulation, the volley of action potentials propagating down the nerve is led by the fastest conducting fibers. Although the rest of the volley contributes to SNAP or CMAP

waveforms, measures of nerve conduction timing (distal latency, conduction velocity, and F- and H-wave latency) focus only on the fastest conducting fibers. . The following is the reference values for normal motor and sensory nerve conduction studies:

No.	**Nerve**	**MNC/ SNC**	**Factors**	**Kimura [64]**	**Misra & Kalita[63]**	**Adams(±2 SD) [60]**
1	Median N.	MNC	Latency(ms)	3.49±0.34	3.77±0.40	< 4.2
			Amplitude(mv)	7.0±3.0	8.10±2.62	>4.4
			Nerve Conduction Velocity (NCV)(m/s)	57.7±4.9	58.52±3.76	>49
			F wave latency(ms)	-	31	<31
		SNC	Latency(ms)	2.84±0.34	3.06±0.41	<3.5
			Amplitude(μv)	38.5±15.6	8.91±4.48	>20
			NCV(m/s)	56.2±5.8	45.45±9.4	>52
2	Ulnar N.	MNC	Latency(ms)	2.59±0.39	2.59±0.40	<3.4
			Amplitude(mv)	5.7±2.0	8.51±2.03	>6.0
			NCV(m/s)	58.7±5.1	61.45±5.73	>49
			F wave latency(ms)	-	31	<32
		SNC	Latency(ms)	2.54±0.29	2.83±0.40	<3.0
			Amplitude(μv)	35.0±14.7	5.54±2.37	>15
			NCV(m/s)	54.8±5.3	54.17±6.10	>52
3	Peroneal N.	MNC	Latency(ms)	3.77±0.86	4.55±0.59	<5.8
			Amplitude(ms)	5.1±2.3	4.23±1.61	>2.0
			NCV(m/s)	48.3±3.9	46.54±4.4	>42
			F wave latency(ms)	-	61	<58
4	Tibial N.	MNC	Latency(ms)	-	-	<6.5
			Amplitude(ms)	-	-	>3.0
			NCV(m/s)	-	48.3±4.5	>41
			F wave latency(ms)	_	61	<59
5	Sural N.	SNC	Latency(ms)	-	-	<4.4
			Amplitude(μv)	-	18.0±10.5	>6
			NCV(m/s)	-	50.9±5.4	>42

Axonal Loss

Axonal loss reduces SNAP and CMAP amplitudes because they represent the summed activity of action potentials. SNAP amplitude is very sensitive to sensory axon loss because there is no compensatory collateral reinnervation. The SNAP originates from ~2000 of the larger diameter nerve fibers (>9 μm in diameter) and amplitude falls rapidly with fiber loss (50% amplitude loss with 50% fiber loss) and is unobtainable with surface recording when ~75% of large fibers lost [36]. However, smaller diameter fibers may remain visible on nerve biopsy. CMAP will be insensitive to mild degrees of motor axon loss because of collateral reinnervation. In slowly progressive disorders, >50—80% of motor nerve fibers can he lost before CMAP amplitude falls below lower limit of normal [27]. Axonal pathology affects conduction velocity measurements (reflected in distal latency, F-wave latency and conduction velocity) in proportion to the number of large fibers lost. Surviving axons will conduct a normal velocities and with normal temporal dispersion.

Conduction Block

Conduction block represents failure of nerve fiber action potentials to conduct beyond a certain point along the axon. This implies that nerve conduction along the fiber is normal on either side of the block. Conduction block can be at a specific site along the nerve (focal conduction block) or at multiple sites along the nerve (multifocal conduction block). Not all fibers in a nerve may be affected (partial vs. complete conduction block). Electrodiagnostic features of focal conduction block are normal conduction distal to the block (normal response amplitude), abnormal conduction across the block (reduced response amplitude), and normal conduction proximal to the block (no further reduction of response amplitude). The magnitude of these changes will vary depending upon how many fibers in the nerve are blocked.

Table: Electrodiagnostic Criteria to Distinguish Focal Conduction Block from Abnormal Temporal Dispersion in Motor Nerves

	CMAP negative peak amplitude	CMAP negative peak area	CMAP negative peak duration
1.Conduction block	<50%	<50%	≤ 30%
2.Conduction block and/or abnormal temporal dispersion	<50%	<50%	>30%
3.Abnormal temporal dispersion	<50%	>50%	>30%

NEEDLE EMG

Needle EMG is an adjunct to nerve conduction studies, and provides data on: (1) the presence of motor axon damage, (2) localization of lesions within the peripheral nervous system and (3) an estimate of the chronicity of motor denervation.

Presence of Motor Axonal Damage

The number of axons that need to be damaged before changes in the clinical examination or CMAP amplitude are apparent varies with the time course of axonal loss. In acute and ongoing disorders, the process of reinnervation will not be able to keep up with the rate of denervation, and clinical and CMAP changes will become apparent relatively early on. In very chronic disorders, the process of reinnervation has sufficient time to reach high capacity, and will be less apparent. Abnormal spontaneous activity (positive sharp waves and fibrillation potentials) represents discharges of single muscle fibers. These potentials represent muscle fiber membrane hypersensitivity due to denervation, and are very sensitive indicator of denervation. Other needle EMG findings focus on the MUAP, and in neuropathic conditions findings include reduced MUAP recruitment, increased amplitude, and increased number of phases and turns.

Localization of Axonal Damage

Nerve conduction studies are most suitable for the study of distal muscles, whereas needle EMG allows assessment of almost any muscle. This allows precise localization of axonal damage to nerve roots, the plexus or single nerves.

Chronicity

Needle EMG also can provide information on the rate of axonal loss. In acute and ongoing processes (recent denervation), fibrillation potentials tend to be large in amplitude (>500 μV). They become smaller as the period between the nerve lesion and the study increases, and may remain of vary small size (<100μV) indefinitely [37]. Accordingly, a pattern of large fibrillation potentials suggests a recent or ongoing process, whereas a pattern of small fibrillation potentials suggests an old or very slowly progressive(chronic) process. Denervated muscle fibers atrophy, and with recent reinnervation, the slower conduction velocity of small diameter muscle fibers contribute to the complexity of MUAPs (polyphasia and polyturns) [38]. With time, reinnervated muscle fibers increase in diameter and motor units become simplified (fewer phases and turns) because of greater temporal dispersion of action potentials making up MUAPs. In static conditions, or slowly progressive conditions, motor unit recruitment will be reduced, MUAP amplitude will be high, but waveforms will be relatively simple [39].

DEMYELINATING POLYNEUROPATHIES

Identifying demyelinating pathology can be difficult, particularly with chronic neuropathies. Nerve biopsy is invasive and is not sensitive for primary demyelination and electrodiagnostic testing, in particular nerve conduction studies, is the most useful diagnostic tool. Sets of nerve conduction criteria have been proposed to distinguish primary demyelination but even with acute inflammatory demyelinating polyradiculoneuropathy (AIDP), whose unique time course helps narrow the differential

diagnosis, only 50% fulfilled criteria when studied within the first two weeks of symptoms. Classic chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is characterized by symmetric proximal and distal motor and sensory nerve involvement [40], but other forms of Chronic demyelinating neuropathies are distinguished, including those with predominant distal nerve involvement [41], asymmetric nerve involvement [42], predominant sensory nerve involvement [43] predominant cranial nerve involvement[44]or focal motor nerve conduction block with and without sensory nerve involvement [45]

Electrodiagnostic Criteria for Demyelination

AIDP and CIDP are the most common examples of multifocal demyelinating polyneuropathies. Findings on motor nerve conduction studies supportive of demyelinating neuropathies include the following: (i)slowed conduction demonstrated by substantially prolonged distal latencies, reduced conduction velocities, and prolonged F- and H-wave latencies; (ii) greater degree of phase cancellation and (iii) sites of focal conduction block (away from common entrapment sites) demonstrated by reduced CMAP amplitude to stimulation proximal to the block with no prolongation of the negative peak duration. Secondary axonal damage also occurs with demyelinating pathology and needle EMG abnormalities are common in AIDP and CIDP [46]

Table: Electrodiagnostic Criteria to Distinguish Primary Demyelinating Pathology from Primary Axonal Pathology in Motor Nerves

Factors	**Electrodiagnostic evidence supportive of primary demyelinating neuropathy**	**Electrodiagnostic evidence supportive of primary axonal neuropathy**
Distal CMAP amplitude	Mild to moderate reduction	Normal to moderate reduction
Conduction block	Present (proximal-to distal CMAP amplitude ratio <0.50)	Absent (proximal-to distal CMAP amplitude ratio >0.50)
Temporal dispersion	Abnormal (proximal-to-distal CMAP negative duration <0.75)	Normal (proximal-to-distal CMAP negative duration >0.75)
	Abnormal (distal negative CMAP duration >9 ms)	Normal (distal negative CMAP duration <9 ms)
Distal latency	Moderately to markedly prolonged (>125% ULN)	Normal to mildly prolonged (<125% ULN)
Conduction velocity	Moderately to markedly slowed (<75% LLN)	Normal to mildly slowed (>75% LLN)
F-wave latency	Moderately to markedly prolonged (>125% ULN)	Normal to mildly prolonged (<125% ULN)
Needle EMG	Mild to moderate denervation	Mild to severe denervation

Sensory Nerve Conduction Studies in Demyelinating Neuropathies

Sensory nerve studies are less useful than motor nerve studies because responses are frequently absent, which do not distinguish between primary demyelination and axonal loss. However, a pattern of an abnormal median is more common in demyelinating neuropathies than in mixed demyelinating and axonal neuropathies [46].

AXONAL POLYNEUROPATHIES

Primary axonal neuropathies are common and generally follow a length dependent pattern [47]. Findings expected on nerve conduction studies for axonal loss include the following: (i) reduced or absent motor and sensory responses, (ii) minimally slowed conduction, and (iii) evidence for neuropathic denervation on needle EMG [48]. Abnormalities will be more severe in lower extremities, with SNAP responses more affected than CMAP responses (due to collateral reinnervation). Axonal loss may be severe, but will have a modest effect on nerve conduction velocity. Needle EMG findings include abnormal spontaneous activity (positive waves and fibrillation potentials) and MUAPs show reduced recruitment and increased amplitude.

MIXED AXONAL AND DEMYELINATING POLYNEUROPATHIES

CIDP will include secondary axonal loss leading to reduced or absent CMAP responses. Diabetes mellitus is the most common cause of distal symmetric polyneuropathies with mixed axonal and demyelinating features. HIV infection may cause similar pattern.

SMALL FIBER NEUROPATHIES

Small fiber neuropathies are clinically defined by symptoms of painful paresthesias in a distal distribution [49]. Sensory and motor responses in the legs are frequently normal, and when abnormal, sensory responses are reduced or absent [50]. The diagnosis of small fiber involvement is confirmed by nerve biopsy showing reduced numbers of unmyelinated fibers, or by skin biopsy showing reduced intraepidermal nerve fiber density.

Materials and Methods

Study Design

This study is a cross sectional study.

Study period

This study was conducted during the period from January 2009 to December 2009, for 1 year. This Study was done in the Department of Neurology, Tirunelveli Medical college Hospital, Tirunelveli.

Patient Selection:

Patients attending the out patient department of Anti Retroviral Therapy (ART) Centre at Tirunelveli Medical College Hospital, Tirunelveli were taken for the study. Patients already diagnosed as HIV positive and on Highly Active Anti Retroviral Therapy (HAART) only were selected for the study. Both male and female patients were taken for the study. Study was done with the consent of the patients.

Inclusion criteria:

1. Patients who were seropositive for HIV infection and registered with ART centre of Tirunelveli Medical College Hospital.
2. Patients on HAART.
3. Both symptomatic and asymptomatic patients.
4. Patients were selected irrespective of stage of the disease, CD4 count and duration of the HIV illness.

Exclusion criteria:

1. HIV seropositive patients who were not on HAART at the time of the study.
2. Patients with other systemic illness like diabetes mellitus, renal disease, thyroid disease, nutritional anaemia, Hansen's disease.

3. History suggestive of collagen vascular diseases, recent Chikunkunya fever or any other viral illness or jaundice.
4. Patients who regularly consume alcohol of > 40 units/week.

All the patients were analysed for,

1. Symptoms of peripheral neuropathy like numbness, tingling, burning pain, pins & needles sensation, muscle thinning, weakness, cramps and other relevant symptoms.
2. If symptoms present, onset and duration of symptoms, whether present before or after starting Anti Retroviral Therapy is noted.
3. Detailed neurological examination for the presence of signs of peripheral neuropathy like diminished touch, pain, temperature and impaired vibration and joint position sensation and muscle wasting, weakness and diminished or absent reflexes.
4. Routine biochemical investigations and complete hemogram to rule out other systemic illness.
5. **Electrophysiological Study**: All the patients were encouraged to undergo nerve conduction study. As many patients refused, study was done in all symptomatic patients and counseling given to remaining asymptomatic patients and at last 5 patients, who were not having symptoms, were willing to undergo electrophysiological study. Totally 30 patient underwent nerve conduction study. The nerve conduction studies were performed with surface recording for sensory and motor nerves. Sensory nerve conduction studies of the sural, ulnar and median nerves were performed orthodromically. Distance was measured from the stimulating cathode to the recording cathode. Measurements included (1) amplitude, in microvolts; (2) latency, in milliseconds; and (3) conduction velocity

(CV), in meters per second. For motor nerve conduction studies, supramaximal nerve stimulation was applied transcutaneously to a distal and proximal segment of the tibial, peroneal, median and ulnar nerves. The compound muscle action potential (CMAP) was recorded with surface disk electrodes. Measurements of the CMAP taken by cursor include (1) amplitude, in millivolts; (2) latency, in milliseconds; and (3) conduction velocity, in meters per second. F-wave latencies were obtained from the median, ulnar, peroneal and tibial motor nerves by recording the minimum latency of 10 responses; at least 10 supramaximal stimuli were applied before it was concluded that F-waves were absent. Electrophysiological diagnosis of peripheral neuropathy was done with standard reference values. [60, 63, 64]

6. The diagnosis of peripheral neuropathy was based on the following criteria: (1) symptoms of peripheral neuropathy (like pain, paresthesias, numbness or weakness in the extremities), (2) neurologic signs (including absent or diminished ankle and or knee reflexes; and reduction of vibratory, pain, or temperature sensation), (3) electrophysiological evidence.

Observations and Results

1. DATA OF STUDY GROUP

Epidemiological data

Total number of patients in our study group is 60. Among them males were 33(55%) and females were 27 (45%).

Table 1.1	MALE	FEMALE	TOTAL
	33 (55%)	27 (45%)	60 (100)

Age Group: Patients were in varying age groups. Minimum of 21 years to maximum of 54 years. Males were aged from 28 to 54 yrs and females were from 21 to 52 yrs.

Table 1.2	GROUP	MINIMUM AGE (YEARS)	MAXIMUM AGE (YEARS)	RANGE (YEARS)
	Total study group	21	54	21-54
	Male	28	54	28-54
	Female	21	52	21-52

More number of patients were in 31-40 yrs (55%) and 21-30 yrs (21.7%) age group.

Table 1.3	AGE GROUP	MALE	FEMALE	TOTAL
	21-30 Yrs	4 (12.1%)	9(33.3%)	13 (21.7%)
	31-40 Yrs	19 (57.6%)	14(51.9%)	33(55.0%)
	41-50 Yrs	8(72.7%)	3(11.1%)	11(18.3%)

	51 Yrs & Above	2(6.1%)	1(3.7%)	3 (5.0%)
	TOTAL	33 (100%)	27 (100%)	60 (100%)

Clinical data

1. Clinical Staging: Patients were staged according to WHO staging system and they were in various stages. More number of patients were in stages III & IV (65%) compared to stages I & II (35%)

Table 1.4

STAGE	NUMBER OF PATIENTS
I	19 (31.7%)
II	2(3.3%)
III	32(53.3%)
IV	7 (11.7%)

Most of the male patients were in stages III & IV and most of the female patients were in stages I & II.

Table 1.5

STAGE	MALE	FEMALE	TOTAL
I	3 (9.1%)	16 (59.3%)	19 (31.7%)
II	1 (3.0%)	1 (3.7%)	2 (3.3%)
II	25 (75.8%)	7 (25.9%)	32 (53.3%)
IV	4 (12.1%)	3 (11.1%)	7 (11.7%)
TOTAL	33 (100%)	27 (100%)	60 (100%)

Chi-square: 18.750; df: 3 **p-value < 0.0001**

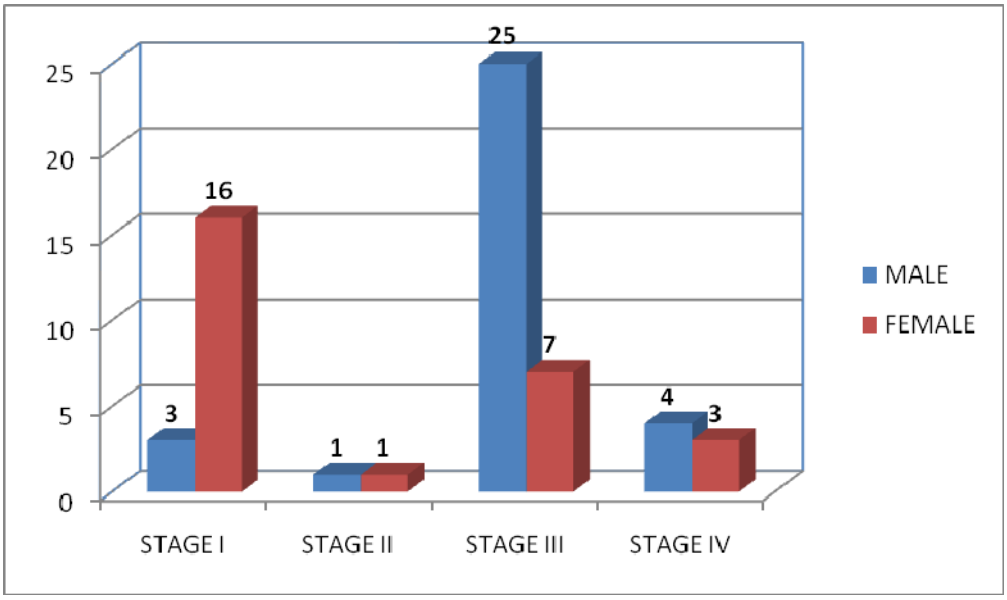

Figure: 1. Clinical Stage and Sex - Multiple Bar Chart

2. Duration of HAART: The duration of HAART varied from 1 – 48 months with mean of 23 months. Those who were on HAART of <12 months were 20, 13-24 months were 19, in 25-36 months were 12, >37 months were 9. Among these, more number of patients 39 (65%) were taking HAART of less than 24 months.

Table 1.6	**DURATION of HAART**	**MALE**	**FEMALE**	**TOTAL**
	0-12 Months	10 (30.3%)	10 (37.0%)	20 (33.3%)
	13-24 Months	11 (33.3%)	8 (29.6%)	19 (31.7%)
	25-36 months	5 (15.2%)	7 (25.9%)	12 (20.0%)
	More than 36 Months	7 (21.2%)	2 (7.4%)	9 (15.0%)
	TOTAL	33 (100%)	27 (100%)	60 (100%)

Chi-square: 3.015 p-value = 0.398.

3. CD4 count: CD4 count was done twice in ART clinic. One at time of diagnosis of HIV seropositivity and one done recently, that is while undergoing this study. Patients having CD4 < 200 are 31(51.7%) > 200 are 29 (48.3%).

Table 1.7	**CD4 < 200**	**CD4 > 200**	**TOTAL**
	31 (51.7%)	29 (48.3%)	60 (100%)

In male patients, those having CD4 less than 200 are 24/33, more than 200 are 9/33 and they were in the range of 35-950. In females those having CD4 less than 200 are 7/27 and more than 200 are 20/27 and they were in the range of 206-1039. Most (72.7%) of the male patients were having CD4 count less than 200.

Table 1.8	**CD4 COUNT (per µl)**	**MALE**	**FEMALE**	**TOTAL**
	CD4 < 200	24 (72.7%)	7 (25.9%)	31 (51.7%)
	CD4 > 200	9 (27.3%)	20 (74.1%)	29 (48.3%)
	TOTAL	33 (100%)	27 (100%)	60 (100%)

Chi-square: 13.025; df: 1 **p-value < 0.0001**

4.Treatment Regimen:

Patients were on various treatment regimens as follows:

REGIMENS OF ART TREATMENT

Table 1.9	REGIMEN		FREQUENCY	PERCENTAGE
		On ATT	1	1.7
		SLE ATT	1	1.7
		SLE SLN	4	6.7
		SLE ZLN	6	10.0
		SLN	12	20.0
		SLN SLE	1	1.7
		SLN ZLN	8	13.3
		ZLE SLN	1	1.7
		ZLN SLN	1	1.7
		ZLE	1	1.7
		ZLE ATT	1	1.7
		ZLE ZLN	8	13.3
		ZLN	15	25.0
		Total	60	100.0

Among them, patients in stavudine group were 56.7% and non-stavudine group were 41.7% and 1 patient was taking ATT at the time of our study.

Table 1.10	STAVUDINE GROUP	NON-STAVUDINE GROUP
	34 (56.7%)	25 (41.7%)

Both males and females were nearly equally present in both groups.

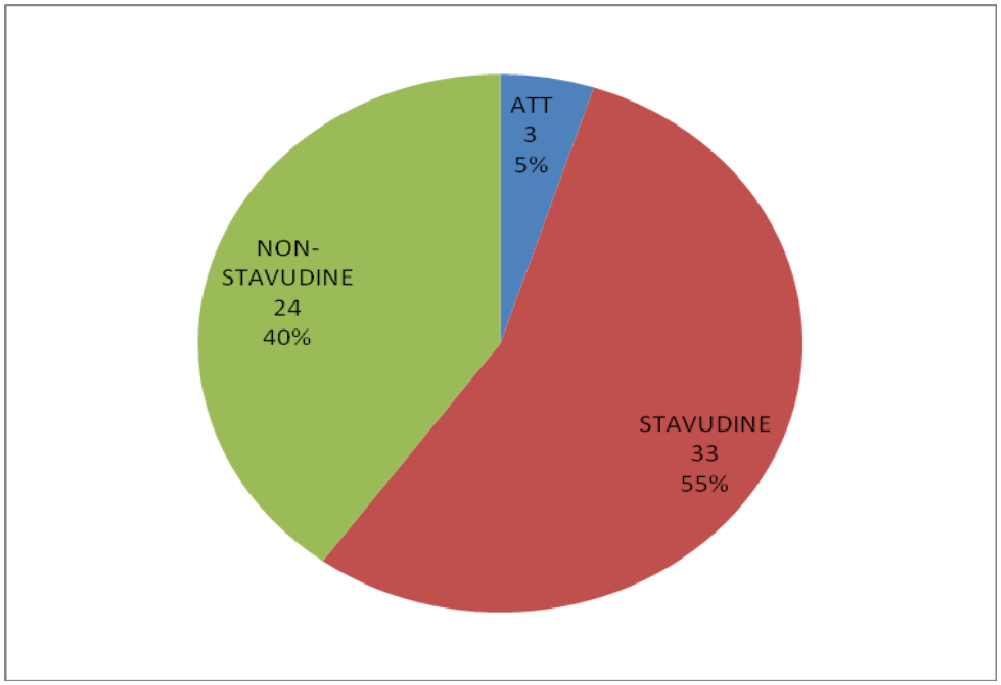

Figure: 2. Treatment Group- Pie Chart

Table 1.11	REGIMEN	MALE	FEMALE	TOTAL
	ATT	1 (3.0%)	0 (0.0%)	1 (1.7%)
	STAVUDINE	17 (51.5%)	17 (63.0%)	34 (56.7%)
	NON-STAVUDINE	15 (45.5%)	10 (37.0%)	25 (41.7%)
	TOTAL	33 (100%)	27 (100%)	60 (100%)

5. Distribution of Symptoms: Among the total number of 60 patients, 23 (38.3%) patients had symptoms of peripheral neuropathy and remaining were asymptomatic.

Table 1.12	SYMPTOMATIC	ASYMPTOMATIC
	23 (38.3%)	37 (61.7%)

Table 1.13	SEX		AGE (years)	DURATION (months)	CD4 COUNT (perμl)
	FEMALE	N	27	27	27
		Minimum	21	2	206
		Maximum	52	42	1039
		Mean	33.22	19.59	508.70
		Std. Deviation	7.708	11.011	220.815
	MALE	N	33	33	33
		Minimum	28	1	35
		Maximum	54	48	950
		Mean	38.00	23.09	351.58
		Std. Deviation	5.590	14.894	250.482
	TOTAL	N	60	60	60
		Minimum	21	1	35
		Maximum	54	48	1039
		Mean	35.85	21.52	422.28
		Std. Deviation	6.991	13.298	248.456

2. DATA OF PERIPHERAL NEUROPATHY GROUP

Among the study group of 60 patients, 26 were having evidence of peripheral neuropathy

Table 2.1	Peripheral Neuropathy PRESENT	Peripheral Neuropathy ABSENT	TOTAL
	26	34	60

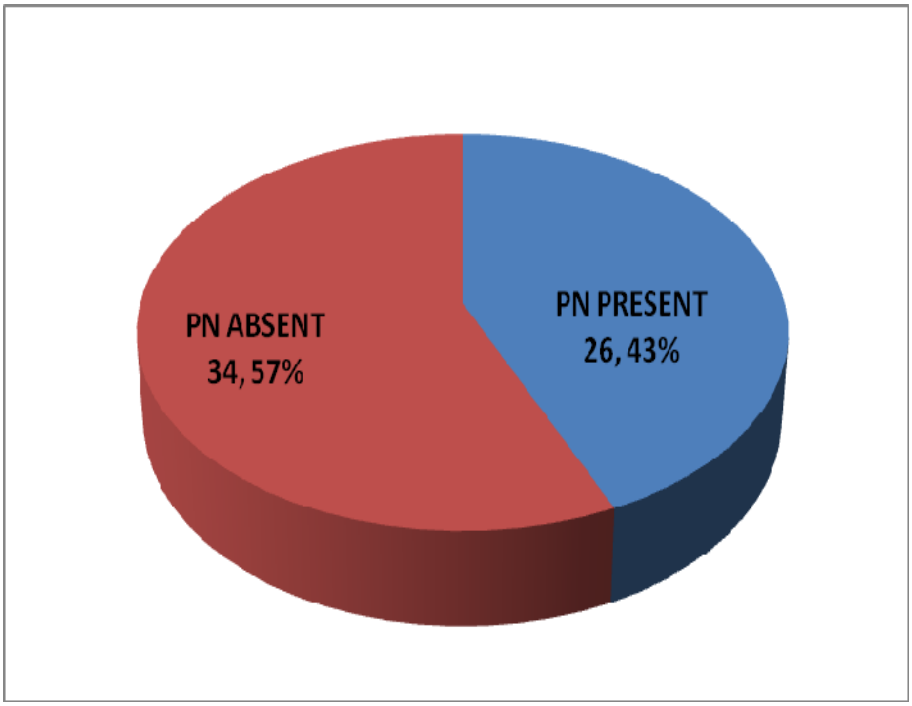

Figure: 3. Peripheral Neuropathy prevalence- Pie Chart

Among the 26 patients with Peripheral Neuropathy, those with Distal Symmetrical Polyneuropathy (DSP) were 18 (69.2%), Distal Sensory Polyneuropathy (Distal Symmetric Polyneuropathy with only sensory findings) were 2 (7.7%), Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) were 5 (19.2%) and Mononeurits Multiplex was 1 (3.8%).

Table 2.2	PERIPHERAL NEUROPATHY – TOPOGRAPHICAL AND CLINICAL TYPES	NUMBER	PERCENTAGE
	CIDP	5	8.3
	Distal Sensory Polyneuropathy	2	3.3
	Distal Symmetric Polyneuropathy	18	30.0
	Mononeuritis Multiplex	1	1.7
	Peripheral Neuropathy - ABSENT	34	56.7
	TOTAL	60	100.0

1. Sex and Peripheral Neuropathy: Among the 26 patients with peripheral neuropathy, 17 (65.4%) were males and 9 (34.6%) were females. Common type seen in both males and females is distal symmetric polyneuropathy.

Table 2.3	Topographical and clinical types of peripheral neuropathy	MALE	FEMALE	TOTAL
	CIDP	4 (23.5%)	1 (11.1%)	5 (19.3%)
	Distal Sensory Polyneuropathy	2 (11.8%)	0 (0.0%)	2 (7.7%)
	Distal Symmetric Polyneuropathy	10 (58.8%)	8 (88.9%)	18 (69.2%)
	Mononeuritis Multiplex	1 (5.9%)	0 (0.0%)	1 (3.8%)
	TOTAL	17 (100%)	9 (100%)	26 (100%)

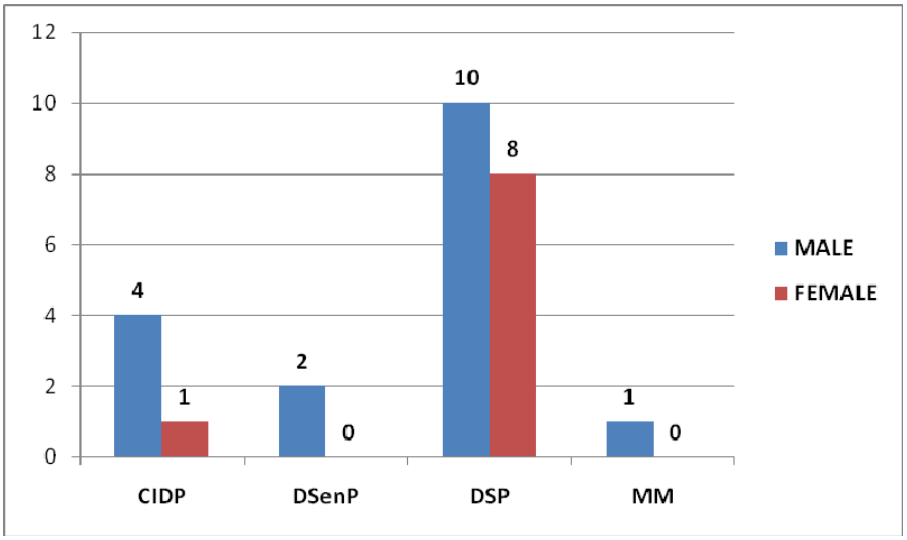

Figure: 4. Sex and Peripheral Neuropathy Types – Multiple Bar Chart

2. Age & Peripheral Neuropathy: Among the 26 patients with PN, they were in different age groups: 21-30yrs – 5 (19.2%), 31-40yrs – 13 (50%), 41-50yrs – 5 (19.2%), >51yrs – 3 (11.5%). More number of patients belonged to 31-40 years age group.

Table 2.4	AGE GROUP	TOTAL	Peripheral Neuropathy – PRESENT	Peripheral Neuropathy - ABSENT	Percentage of peripheral neuropathy
	21-30 Yrs	13(21.7%)	5 (19.2%)	8 (23.5%)	38.5 %
	31-40 Yrs	33 (55.0%)	13 (50.0%)	20 (58.8%)	39.4 %
	41-50 Yrs	11 (18.3%)	5 (19.2%)	6 (17.6%)	45.5 %
	51 Yrs & Above	3 (5.0%)	3 (11.5%)	0 (0.0%)	100 %
	TOTAL	60	26	34	

Chi-square: 4.277 p-value: 0.233.

3. Stage of disease and Peripheral Neuropathy: More number of patients (19 out of 26 or 71.1%) were in stages III & IV, compared to stages I & II (7 out of 26 or 28.9%). In the study group, 39/60 were in stages III & IV and 21/60 were in stages I & II. Among the 39 patients of stage III & IV, 19 (48.7%) suffers from peripheral neuropathy and among the 21 patients of stage I & II, 7 suffers from peripheral neuropathy.

Table 2.5

STAGE	Peripheral Neuropathy – PRESENT	Peripheral Neuropathy - ABSENT	TOTAL
I	6 (23.1%)	13 (38.2%)	19 (31.7%)
II	1 (3.0%)	1 (2.9%)	2 (3.3%)
III	15 (55.7%)	17 (50.0%)	32 (53.3%)
IV	4 (15.4%)	3 (8.8%)	7 (11.7%)
TOTAL	26	34	60

Chi-square: 1.812 p-value = 0.612

4. Duration of HAART and Peripheral Neuropathy: Among the 26 patients, those who were on HAART of 0-12 months are 12 (46.2%), 13-24 months are 6 (23.1%), 25-36 months are 4 (15.4%) and more than 36 months are 4 (15.4%). Among the 39 patients of less than 24 months, 18 (46.2%)suffers from peripheral neuropathy and among the 21 patients of more than 24 months, 8 (38.1%)suffers from peripheral neuropathy.

Table 2.6	Duration of HAART	Total no. of patients	Peripheral Neuropathy - PRESENT	Peripheral Neuropathy - ABSENT	percentage
	0-12 Months	20 (33.3%)	12 (46.2%)	8 (23.2%)	60%
	13-24 Months	19 (31.7%)	6 (23.1%)	13 (38.2%)	31.6%
	25-36 months	12 (20.0%)	4 (15.4%)	8 (23.5%)	33.3%
	> 36 Months	9 (15.0%)	4 (15.4%)	5 (14.7%)	44.4%
	TOTAL	60	26	34	

Chi-square: 3.825 p-value = 0.281

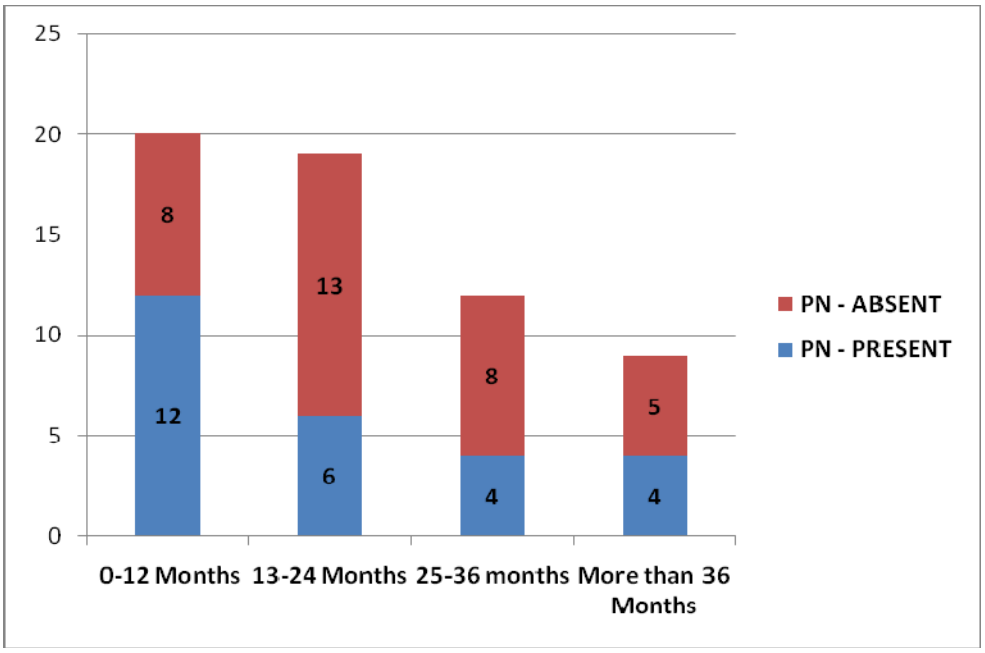

Figure: 5. Duration of HAART and Peripheral Neuropathy – Component Bar Chart

5. CD4 count and Peripheral Neuropathy: Those patients with peripheral neuropathy with CD4 < 200 were 9 (34.6%), and > 200 were 17 (65.4%). In total study group, patients with CD4 < 200 were 31 (51.7%) and > 200 were 29

(48.3%). This shows no increased risk of developing PN for those patients with less CD4 count. But it is not statistically significant**.**

Table 2.7	**CD4 < 200/µl**	**CD4 > 200/µl**
	9 (34.6%)	17 (65.4%)

6. Regimen group and Peripheral Neuropathy: Among the 26 patients with peripheral neuropathy, 16 (61.5%) were in stavudine group and 1 was taking ATT and remaining 9 (34.6%) were in non-stavudine group.

Table 2.8	**REGIMEN GROUP**	**Peripheral Neuropathy - PRESENT**	**Peripheral Neuropathy - ABSENT**	**TOTAL**
	ATT	1 (3.8%)	0 (0.0%)	1 (1.7%)
	STAVUDINE	16 (61.5%)	18 (52.9%)	34 (56.7%)
	NON-STAVUDINE	9 (34.6%)	16 (47.1%)	25 (41.7%)
	TOTAL	26	34	60

Chi-square: 2.047; df: 2; p-value = 0.359.

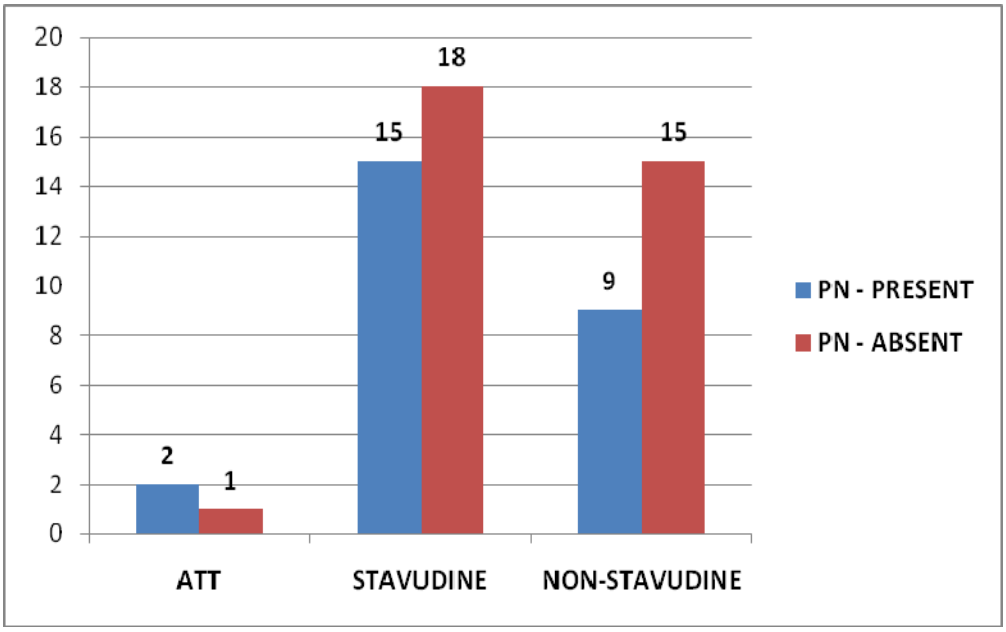

Figure: 6. Regimen Group and Peripheral Neuropathy – Multiple Bar Chart

Among these 26 patients with peripheral neuropathy, when correlating duration of HAART with regimen and CD4 cell count, it shows the following results:

	Duration of HAART	No. of peripheral neuropathy patients				
		Regimen		CD4 cell count/µl		
		On Stavudine	On Non-Stavudine	Less than 200	More than 200	Total
Table 2.9	0 – 12 months	5	7	4	8	12
	13 – 24 months	4	2	3	3	6
	25 – 36 months	3	1	2	2	4
	> 36 months	4	Nil	2	2	4
	Total	16	10	11	15	26

Table 2.10	Duration of HAART	Total no. patients	Stavudine users (A)	Peripheral neuropathy present in (A)	Non-stavudine users (B)	Peripheral neuropathy present in (B)
	0-12 months	20	10	5 (50%)	10	7 (70%)
	13-24 months	19	10	4 (40%)	9	2 (22.2%)
	25-36 months	12	8	3 (37.5%)	4	1 (25%)
	> 36 months	9	6	4 (66.7%)	3	Nil
	Total	60	34	16 (47.1%)	26	10 (38.5%)

Table 2.11	Stage of disease	Stavudine users(A)	Peripheral neuropathy present among(A)	Non-stavudine users(B)	Peripheral neuropathy present among(B)
	I & II	10	4 (40%)	11	4 (36.4%)
	III	18	9 (50%)	14	6 (42.9%)
	IV	6	3 (50%)	1	0
	Total	34	16	26	10

7. Analysis of symptomatic patients

Among the 26 patients with peripheral neuropathy, 23 patients (88.5%) had both symptoms and signs of peripheral neuropathy and 2 patients, showed signs of peripheral neuropathy during clinical examination and nerve conduction study also confirmed this.

Table 2.12	Symptoms and signs present	Only signs present	Only electrophysiological evidence present
	23/26 (88.5%)	2/26 (7.7%)	1/26 (3.8%)

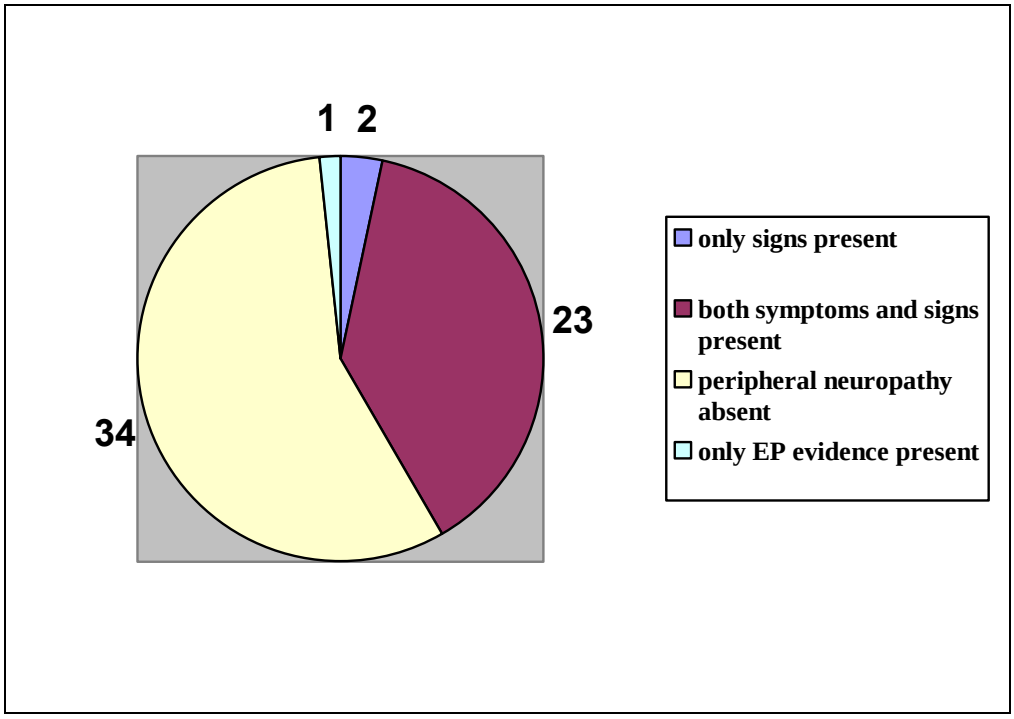

Figure: 7. Distribution of symptoms and signs – Pie Chart

Patients, who didn't have either symptoms or signs of peripheral neuropathy, were 35. Among them 5 underwent electrophysiological analysis. One of them showed electrophysiological evidence of peripheral neuropathy.

Table 2.13	Total No. of patients	Not having either symptoms or signs (B)	Underwent Electrophysiology study among (B)	Electrophysiology evidence of Peripheral Neuropathy seen in
	60	35	5	1

All the symptomatic patients had electrophysiological evidence of peripheral neuropathy and this is statistically significant as p-value is < 0.0001.

Table 2.14	SYMPTOMS	Peripheral Neuropathy – PRESENT	Peripheral Neuropathy - ABSENT	TOTAL
	PRESENT	23 (88.5%)	0 (0.0%)	23 (38.3%)
	ABSENT	3 (11.5%)	34 (100%)	37 (61.7%)
	TOTAL	26	34	60

Chi-square: 48.773 **p-value <0.0001**

Sensitivity: 88.5%; Specificity: 100%; PPV: 100%; NPV: 91.9%

8. Analysis of Symptoms: Frequent symptoms we encountered were numbness (17 patients), tingling (8 patients) and electric shock-like sensation (5 patients) and less frequent symptoms were burning pain (3 patients) and pins and needles sensation(5 patients). Some patients (4 patients) had cramps in both legs. Only few patients (2 patients) showed weakness.

Table 2.15	SYMPTOM	No. OF PATIENTS
	Numbness	17
	Tingling	8
	Pins & needles	5
	Burning pain	3
	Both tingling & burning	4
	Cramps	4
	Weakness	2

Most of the patients showed symptoms in lower limbs (20 patients). Only in 5 patients symptoms were present in both upper and lower limbs.

Table 2.16	SYMPTOMS	No. OF PATIENTS
	Only in lower limbs	20
	Both lower & upper limbs	5

9. Sensory signs: Sensory signs, seen in our study were diminished vibration, touch, pain and temperature in that order. Mostly these were present below the ankles and only in some patients below the knees. In few patients, especially in CIDP group signs were present in hands. In 17 patients all modalities like vibration, touch, pain and temperature were lost in lower limbs. In 8 patients only vibration impairment was seen. In 3 patients sensory signs (impairment of vibration) were present in hands.

Table 2.17	SENSORY IMPAIRMENT	NO. OF PATIENTS
	Impairment of vibration, touch, pain and temperature	17
	Only impairment of vibration	8

10. Motor signs: Ankle jerk was diminished in 6 patients and absent in 11 patients. 4 patients had diminished knee jerk. Weakness in ankle dorsiflexion and plantar flexion were seen in 2 patients, weakness in extension of great toe was present in 4 patients and in 7 patients toe-grip was weak. Wasting seen in intrinsic foot muscles in 3 patients. In upper limbs, signs were not seen except in patients with CIDP (Chronic Inflammatory Demyelinating Polyneuropathy) who showed both sensory and motor features. Like wise CIDP patients had both proximal and distal weakness in lower limbs.

Table 2.18	SIGNS	NO. OF PATIENTS
	Diminished ankle jerk	6
	Absent ankle jerk	11
	Diminished knee jerk	4
	Weakness of ankle dorsiflexion and plantar flexion	2
	Weakness in extension of great toe	4
	Toe grip weakness	7
	Wasting in extremities	3

11. Electrophysiology

Nerve conduction study was done totally in 30 patients. Among them, electrophysiological evidence of peripheral neuropathy was seen in 26 patients. Predominant pattern seen was mixed neuropathy (both axonal and demyelination) in 18 patients. Among the 5 patients with CIDP, 1 patient had features of both axonal and demyelination pattern and others had predominant demyelination pattern. 3 patients had only axonal pattern. Both motor and sensory neuropathy were seen in 24 patients and only sensory neuropathy was seen in 2 patients.

Table 2.19	PATHOLOGICAL PATTERN OF NEUROPATHY	NO. OF PATIENTS
	Axonal	3
	Demyelinating	5
	Both axonal & demyelination	18

Distribution of Neuropathy: In 13 patients electrophysiological evidence of peripheral neuropathy was seen in both upper limbs and lower limbs. In remaining 13 patients only in lower limbs peripheral neuropathy was present. In patients with distal symmetric

polyneuropathy, electrophysiological evidence was predominantly seen in lower limbs (13 patients) and in remaining 7 patients was seen both in upper limbs and lower limbs.

Table 2.20	**Electrophysiological evidence of peripheral neuropathy seen in**	**No. of patients**
	Only in lower limbs	13
	Both upper & lower limbs	13

The following table analyses the correlation between the peripheral neuropathy and age of the patients, duration of HAART and CD4 count.

Table 2.21	**PERIPHERAL NEUROPATHY**		**AGE (years)**	**DURATION of HAART(months)**	**CD4 COUNT**
	PRESENT	N	26	26	26
		Minimum	21	1	35
		Maximum	54	48	950
		Mean	37.62	19.15	367.85
		Std. Deviation	7.874	14.603	247.253
	ABSENT	N	34	34	34
		Minimum	23	2	66
		Maximum	46	48	1039
		Mean	34.50	23.32	463.91
		Std. Deviation	6.006	12.117	244.811
	TOTAL	N	60	60	60
		Minimum	21	1	35
		Maximum	54	48	1039
		Mean	35.85	21.52	422.28
		Std. Deviation	6.991	13.298	248.456

The following table shows the statistical analysis of peripheral neuropathy with various factors.

Table 2.22

FACTOR	Peripheral Neuropathy – PRESENT (N= 26)	Peripheral Neuropathy – ABSENT (N= 34)	ODDS RATIO	Chi-square	p-value
AGE > 36 Yrs	19 (73.1%)	15 (44.1%)	3.48	5.032	**0.025**
SEX -MALE	17 (65.4%)	16 (47.1%)	1.37	1.999	0.157
DURATION ≥ 22 MONTHS	11 (42.3%)	19 (55.9%)	0.58	1.086	0.297
SYMPTOM OF PERIPHERAL NEUROPATHY	23 (88.5%)	0 (0.0%)	21.3	48.77	**0.000**
CLINICAL STAGE –III&IV	19 (73.1%)	20 (58.8%)	1.24	1.321	0.251
CD4 COUNT ≤ 200	12 (46.2%)	19 (55.9%)	0.67	0.558	0.455

increasing age and advanced clinical stages are significantly associated with more prevalence of peripheral neuropathy.

Discussion

This study is a cross sectional study done to estimate the prevalence and to evaluate the risk factors, types and pattern of peripheral neuropathy in HIV infected individuals in our region.

1. Analysis of the study group

In this study, a survey of variables related to peripheral nerve function in the group of HIV-infected individuals in whom nerve conduction studies and several potential pathogenetic factors have been systematically studied.

In our study group, among the total number of 60 patients, 33(55%) were males and 27 (45%) were females (Ref. Table 1.1). Patients with varying age group were included in our study from 21 years to 54 years. Males were aged from 28 to 54 yrs and females from 21 to 52 yrs. More number of patients were in 31-40 yrs age group (55%) followed by 21-30 yrs (21.7%) age group. (Ref. Table 1.3)

They were in various stages of disease from stage I to stage IV (Ref. Table 1.4, 1.5) The staging was done based on WHO staging at the time of the diagnosis of the disease. There were 19 patients in stage I, 2 patients in stage II, 32 patients in stage III and 7 patients in stage IV. More number of the males were in the advanced stages (29 – 87.9% in stages III & IV) as compared to females (10 – 37.0% in stages III & IV). The difference was statistically significant (p- value < 0.0001).

The duration of the patients on HAART varied from 1 – 48 months with mean of 23 months (Ref. Table 1.6). Those who were on HAART of <12 months were 20 (33.3%), 13-24 months were 19 (31.7%), in 25-36 months were 12 (20.0%), >37 months were 9 (15.0%).

CD4 count value was taken from medical records and two counts were noted. One at the time of diagnosis of HIV seropositivity and another one done recently, that is while doing examination. Patients having CD4 < 200 were 31(51.7%) and > 200 were 29 (48.3%) (Ref. Table 1.7, 1.8). In male patients, those having CD4 less than 200 were 24/33 (72.7%), more than 200 were 9/33 (27.3%). In females those having CD4 less than 200 were 7/27 (25.9%) and more than 200 were 20/27 (74.1%). The males had less CD4 count as compared to females. The difference is statistically significant (p- value < 0.0001)

Patients were on various regimen groups. In the ART centre attached to our hospital, 4 types of regimens are followed, which contain 2 NRTIs and 1 NNRTI. The following regimens are used. ZLN, ZLE, SLN, SLE (Z – zidovudine, L – lamivudine, S – stavudine, N – nevirapine, E – efavirenz). Among NRTIs lamivudine is compulsorily added and either zidovudine (if no anemia) or stavudine (if no PN) is added. Among NNRTIs either nevirapine (if no ATT or hepatotoxicity) or efavirenz (if nevirapine contraindicated) is used. Some patients who were suffering from PT were started on ATT first and then after completing ATT, later started on HAART and in between also if PT is detected, HAART stopped and ATT started and HAART restarted later. Totally 23 such patients were given ATT at one point of time. Among whom one was presently on ATT at the time of our study (Ref. Table 1.9, 1.10, and 1.11).

Patients who were on stavudine regimen were 34 (56.7%). Remaining were on non-stavudine regimen 26 (43.3%). Among the drugs used as HAART, the'd' drugs (didanosine, zalcitabine, stavudine) are prone to produce neurotoxicity. In our ART centre stavudine is used and other 2 drugs are not used. So patients were divided into those on stavudine (stavudine group) and not on stavudine (non-stavudine group).

2. Analysis of Peripheral Neuropathy Group

Among the 60 patients under the study, 26 patients were having peripheral neuropathy and electrophysiological study confirmed the condition.

1. Types of Peripheral Neuropathy: Among the 26 patients with peripheral neuropathy those with distal symmetrical polyneuropathy (DSP) were 18 (69.2%), distal symmetric polyneuropathy with only sensory findings (Distal Sensory Polyneuropathy) were 2 (7.7%), CIDP were 5 (19.2%) and Mononeuritis Multiplex (MM) was 1 (3.8%) (Ref. Table 2.2). Among the inflammatory demyelinating polyneuropathies, both AIDP (acute inflammatory demyelinating polyradiculoneuroathy) and CIDP (chronic inflammatory demyelinating polyradiculoneuropathy) can occur in HIV infected patients [66]. Acute form often presents at the time of HIV seroconversion or primary infection. But we did not encounter AIDP though we had 5 patients of CIDP. This may be because of the method of patient selection. We selected patients from out patient department of ART centre where they come for follow up and getting drugs. Acutely ill AIDP patients could have been admitted and treated either in the intensive medical care unit or in the medical units. Other types described in text books and literature [66, 74] like progressive polyradiculopathy, autonomic neuropathy and mononeuropathy were not seen in our study, as noted in other Indian study [68].

In our study, distal symmetric polyneuropathy was the common type (76.9%), even after exclusion of patients with confounding factors for distal peripheral neuropathy, like diabetes mellitus and alcoholism, an observation similar to those described in literature [71]. As this distal symmetric polyneuropathy can occur due to HAART as well as due to ATT, it needs prospective analysis to find out whether it is drug induced. Overall, among the total number of study group of 60 patients, distal symmetric polyneuropathy seen in 20 patients (33.3%) similar to described in other series [69].

2. Age & Peripheral Neuropathy: Among the 26 patients with peripheral neuropathy, they were in different age groups: 21-30yrs – 5 (19.2%), 31-40yrs – 13 (50%), 41-50yrs – 5 (19.2%), >51yrs – 3 (11.5%) (Ref. Table 2.4). When comparing this with total study population of same age group, prevalence gradually increases from 38.5% to 100%. (Ref.Table.2.4). This shows the prevalence increases as age advances as seen in other studies [76]. But it is not statistically significant (p- value= 0.233). . An article reviewing the impact of aging in HIV infection and its neurological complications [75] explains that aging is associated with a higher viral load and immunosenescence, with a decrease in the naive subsets of CD4 cells, decreases in T cell proliferative responses and decreased ability to respond to novel pathogens, resulting in a potential synergism between HIV infection and aging.

3. Sex and Peripheral Neuropathy: Among the 26 patients with peripheral neuropathy, 17 (65.4%) were males and 9 (34.6%) were females (Ref. Table 2.3). When comparing this with overall study group (60 patients) also males are more affected (17/33 or 51.5%) than females (9/27 or 33.3%). That shows peripheral neuropathy more in male patients. But statistically it is not significant.

4. Duration of HAART and Peripheral Neuropathy: Among the 26 patients, those who were on HAART of < 24 months are 18 (69.2%), whereas more than > 24 months are 8 (30.8%) (Ref. Table 2.6). When taking the total study population into account, prevalence of peripheral neuropathy gradually decreases from 60% (in 0-12 months duration of HAART) to 44.4% (in more than 36 months of HAART) (Ref. Tab.2.6). This indicates that longer duration of HAART reduces the chance of developing peripheral neuropathy. HAART lessens disease progression, improves immunity, and widens the ratio of therapeutic to toxic effects of individual antiretroviral drugs, resulting in a significantly lower risk of developing peripheral neuropathy [74].

5. Treatment regimen and Peripheral Neuropathy: Among the 26 patients with peripheral neuropathy, 16 (61.5%) were on stavudine regimen and 1 was taking ATT and remaining 9 (34.6%) were on non-stavudine regimen. When comparing this with total study population of 60 patients, peripheral neuropathy seen in stavudine users is 47.1% (16/34) and in non-stavudine user is 36% (9/25) (Ref. Table 2.8). This shows more number of peripheral neuropathy in stavudine users. This observation is similar to the findings seen in other studies [73]. But it is not statistically significant as p-value is 0.359. Another observation is that in all the stages of the disease, peripheral neuropathy is slightly more in stavudine users (Ref. Table.2.9, 2.10). This suggests the possibility of drug toxicity of the stavudine is an added factor for the development of peripheral neuropathy in all the stages.

Interestingly in less than 12 months duration of HAART, peripheral neuropathy patients on stavudine regimen were 5 and on non-stavudine regimen were 5 (excluding 1 patient on ATT and another one was on ZLE & ATT). That is, at the time of seroconversion, peripheral neuropathy seen equally in both stavudine and non-stavudine regimen. In 13-24 months duration of HAART, patients on stavudine regimen were 4 and on non-stavudine regimen were 2. In 25-36 months duration of HAART, patients on stavudine regimen were 3 and non-stavudine regimen was 1. In more than 36 months of HAART, patients on stavudine were 4 and none was on non-stavudine regimen (Ref. Table.2.9). This indicates that peripheral neuropathy in the initial period of seroconversion may be due to the disease process because irrespective of the type of regimen used, peripheral neuropathy was seen and in peripheral neuropathy of later period, may be due to drug toxicity, because peripheral neuropathy was seen only in stavudine users. This is supported by the evidence that peripheral neuropathy seen in more than 36 months of HAART group was associated with increased CD4 count in 2 of

4 patients (Ref. Table2.9). (suggestive of improved immunological status). So peripheral neuropathy in that duration of HAART might be due to neurotoxicity of stavudine. However, this is a study of small group and this needs to be evaluated with large number of patients.

6. Stage of disease and Peripheral Neuropathy: More number of patients (19 out of 26 or 71.1%) were in stages III & IV, compared to stages I & II (7 out of 26 or 28.9%) (Ref. Table 2.5). In total number of study group, 39 (out of 60) were in stages III & IV and 21 (out of 60) were in stages I & II. When comparing these two data, increased risk of developing peripheral neuropathy in advance stages (stage III & IV: 48.7% or 19/39 and stages I & II: 33.3% or 7/21), an observation similar to other studies [69].But it is not statistically significant in our study (p-value: 0.612).

7. CD4 count and Peripheral Neuropathy: Those with peripheral neuropathy with CD4 < 200 are 9 (34.6%), and > 200 are 17 (65.4%) (Ref. Table 2.7). In total study group, patients with CD4 < 200 are 31 (51.7%) and > 200 are 29 (48.3%). This shows no increased risk of developing peripheral neuropathy for those patients with less CD4 count. But it is not statistically significant. Peripheral neuropathy patients with CD4 count more than 200 suggest that peripheral neuropathy may be due to drug toxicity or other underlying conditions as described in literature [9].

8. Analysis of symptoms: Frequent symptoms we came across were numbness (17/23), tingling (8/23), electric shock like sensation (5/23) with less frequently burning pain (3/23), pins and needles (5/23) (Ref table 2.15). Our findings are comparable with those reported in previous studies, in which subjective pain was uncommon and usually present in more advanced stages [26, 72]. These observations are similar to that reported in other studies [69]. Some patients (4) had cramps in both legs, as reported in some other series [69], which could be due to motor neuropathy or metabolic or drug related and could not

be differentiated. Most (20/25) of the patients had symptoms in lower limbs. Only in 5 patients, symptoms were present in hands and legs. But electrophysiological study picked up the presence of peripheral neuropathy in upper limbs in some patients who had signs only in lower limbs. This indicates the presence of subclinical neuropathy in asymptomatic sites.

9. Analysis of signs: Sensory signs: Sensory signs seen in our study were diminished vibration, touch, pain and temperature in that order. Mostly signs were present below ankle, and in some patients below knee. Only in few patients, especially in CIDP group signs were present in hand. In 17 patients all modalities like vibration, touch, pain and temperature were lost in lower limbs. In 8 patients, only vibration impairment was seen (Ref.Table.2.17). In 3 patients, sensory signs were present in hands, mainly vibration impairment.

Motor signs: Predominant motor sign was abnormal ankle jerk, which was diminished in 6 patients and absent in 11 patients. In some patients (4 patients), diminished knee jerk was noted. Weakness in ankle dorsiflexion and plantar flexion was seen in 2 patients, weakness in extension of great toe seen in 4 patients and in some (7 patients), toe-grip was weak (Ref table 2.18) and in 3 patients, wasting in foot intrinsic muscles was seen. In upper limbs, signs were not seen except in 2 CIDP patients, who showed both sensory and motor findings. Like wise CIDP patients had both proximal and distal weakness in lower limbs. Both sensory and motor signs present in our study are similar to what described in literature [66].

10. Electrophysiological study:

Nerve conduction study was done only in 30 (50%) patients as many patients refused for nerve conduction study. Only those patients, who were having symptoms of peripheral neuropathy, were willing to undergo electrophysiological study.

Among 60 patients, 23 patients (38.3%) had both symptoms and signs of peripheral neuropathy and 2 patients, even though did not have symptoms, showed signs of peripheral neuropathy on clinical examination nerve conduction study confirmed this.

Among those patients who neither had symptoms nor signs of peripheral neuropathy, 5 patients were studied after counseling them and 1 of these 5 patients (20%) showed electrophysiological evidence of peripheral neuropathy. This indicates subclinical neuropathy may be present in 20% of HIV infected patients. However this is a group of small number and it has to be evaluated with large number of patients.

In those patients who were having symptoms of peripheral neuropathy (23/26), all had clinical and Electrophysiological evidence of Peripheral Neuropathy (p-value: 0.0001) (sensitivity 88.5%). And 2 patients who didn't have symptoms, but showed signs on examination. And all 25 patients with signs of peripheral neuropathy were having electrophysiological evidence of peripheral neuropathy. So detailed history and neurological examination is necessary in all HIV infected patients.

Nerve conduction study was done totally in 30 patients. Among them, electrophysiological evidence of peripheral neuropathy was seen in 26 patients. Predominant pattern seen was mixed neuropathy (both axonal and demyelination), which was seen in 18 patients. (Ref table 2.19) But in literature predominant pattern seen is Axonal [53, 67]. Among the 5 patients with CIDP, 1 patient had features of both axonal and demyelination pattern and others showed predominant demyelination pattern. 3 patients showed only axonal pattern. Both motor and sensory neuropathy was seen in 24 patients and only sensory neuropathy was seen in 2 patients.

In 13 patients, electrophysiological evidence of peripheral neuropathy was seen in both upper limbs & lower limbs. In remaining 13 patients, only in lower limbs peripheral neuropathy features were present. But clinically many (20/23) had symptoms only in

lower limbs. (Ref table 2.20) It shows subclinical peripheral neuropathy may be present in upper limbs. In patients with distal symmetric polyneuropathy, electrophysiological evidence was predominantly seen in lower limbs (13 patients) and in remaining 7 patients was seen both in upper limbs and lower limbs.

Comparing our study with other Indian study:

NO	FACTOR	JYOTI GARG ET AL [53]	OUR STUDY
1.	Total no. of patients	39	60
2.	Peripheral Neuropathy present in	20	26
3.	Mean duration of HAART(months)	24	19
4.	CD4 < 200	17	9
	> 200	3	17
5.	Symptoms seen in	20 (100%)	23 (88%)
6.	Signs seen in	20 (100%)	25 (96%)
7.	Electrophysiological evidence of Peripheral Neuropathy seen	4/20	26/26
8.	Pattern of Peripheral Neuropathy	Distal symmetric polyneuropathy. Axonal pattern	Commonly distal symmetric polyneuropathy, others:CIDP,MM. Mixed pattern (both axonal and demyelinating)
9.	No. of patients on HAART	17/20	26/26
10.	Correlation between duration of HAART and peripheral neuropathy	No significant relation	less number of peripheral neuropathy patients seen in longer duration of HAART

Comparing our study with other international studies:

NO.	FACTOR	BRAZIL STUDY [52]	NEUROPHYSIOLOGIC CLINIC DEC.1987 [51]	OUR STUDY
1.	Total no. of patients	49	41	60
2.	M : F	32 : 17	-	33 : 27
3.	Mean age	36.8	-	35.6
4.	Age range (years)	21-53	-	21-54
5.	Peripheral Neuropathy seen in	34 (69.4%)	36 (88%)	26 (43.3%)
6.	Both symptoms and signs seen in	12/34	-	23/26
7.	Only signs seen in	22/34	-	2/26
8.	Subclinical (no symptoms, no signs) Peripheral Neuropathy	2	17	1/26
9.	Neurotoxic drug intake	32 (94.1%)	-	18 (69.2%)
10.	Electrophysiological study done in	39	-	30
11.	Peripheral Neuropathy seen in (among those underwent Electrophysiology)	13/39	-	26/30
12.	Common type seen	Distal Symmetric Polyneuropathy (8/13)	Distal Symmetric Polyneuropathy	Distal Symmetric Polyneuropathy (20/26)

Some observations of our study go along with other studies. [55, 56] For example the common type distal symmetric polyneuropathy seen in other studies [51,52,53] is also the common type in our study. Prevalence seen in our study is similar with other studies [69,70]. Unlike other studies [53], in our study, those having symptoms and signs were having electrophysiological evidence of peripheral neuropathy. In our study, male sex, advanced stage of disease and increasing age are associated with more risk of developing peripheral neuropathy (Ref. Table 2.22). Also those on HAART of longer duration are

less affected with peripheral neuropathy. But these observations are not statistically significant. Only the positive symptom by history and increasing age are significantly associated with the occurrence of peripheral neuropathy. Like other studies [69] CD4 count doesn't correlate with prevalence of peripheral neuropathy.

Summary

1. Prevalence of peripheral neuropathy in HIV infected patients in our study is 26/60 (43.3%).
2. In our study, peripheral neuropathy is seen more in patients with advanced clinical stage and increasing age. There is no increase in prevalence of peripheral neuropathy in patients with less CD4 count. But these observations, except the age of the patients, are not statistically significant.
3. Peripheral neuropathy less commonly seen in patients on HAART of longer duration. As duration of HAART increases, peripheral neuropathy is seen more in stavudine users, suggesting drug toxicity is the cause for peripheral neuropathy rather than HIV-related. But this needs to be confirmed with neuropathological studies.
4. Distal symmetrical polyneuropathy is the common type (20/26). Common pathological pattern of neuropathy is mixed (both axonal and demyelination) neuropathy (18/26).
5. All patients who had symptoms of peripheral neuropathy had electrophysiological evidence of peripheral neuropathy. Likewise all patients with signs of peripheral neuropathy had electrophysiological evidence of peripheral neuropathy. Hence detailed history and clinical examination for symptoms and signs of peripheral neuropathy is essential in all HIV infected patients as it can pick up more number of patients with peripheral neuropathy earlier and so they can be treated earlier.

6. Among the 5 patients (who didn't have either symptoms or sings of peripheral neuropathy) who underwent nerve conduction study, 1 had electrophysiological

evidence of peripheral neuropathy. So subclinical peripheral neuropathy present in 20% (1/5) of patients. But this needs to be evaluated with large number of patients.

7. Numbness and tingling were the common and burning pain and pins and needles sensations were the less common symptoms seen in our patients. Diminished or absent ankle jerks, impaired vibration, touch, pain and temperature were the common signs.
8. Symptoms and signs were more common in lower limbs than in upper limbs.

Dissertation on Peripheral Neuropathy in HIV Infected Patients

Master Chart (1)

S. No.	Pt's Name	Age (Y) / S	ART Centre No	Regimen	Duration	Stage at Diagnosis	past H/O any illness	Any other drug intake	Symptoms of PN		Signs of PN	Investigations - Blood						CD4 Count/µl		NCS	Inference
									Yes/No	Duration		Sugar [R] (mg%)	Urea (mg%)	Creati. (mg%)	Hb (gm%)	TC (C/cumm)	PS-megalob last	AT Diag.	Recent		
1	Perumal	30/M	45/07	ZLN	2Y	III	Nil	Nil	N	-	Nil	74	18	0.9	14	6000	Nil	172	402	ND	Not Sugg. of PN.
2	Murugan	39/M	387/07	ZLE ZLN	1Y3M	III	Nil	Nil	Y	3M	Y	79	17	1.0	11.7	7100	Nil	75	328	D	DSP
3	Periyathai	32/F	348/07	SLN ZLN	2Y	I	Nil	Nil	N	-	Nil	63	18	1.0	12.6	4100	Nil	169	414	ND	Not Sugg. of PN.
4	Mariappan	39/M	147/09	On ATT	5M	III	Nil	ATT	Y	3M	Y	109	29	1.2	12.7	4300	Nil	70	35	D	DSP
5	Kathirvel	40/M	35/09	ZLE ZLN	3M	III	Nil	Nil	Y	6M	Y	88	19	1.5	11.4	5400	Nil	117	950	D	CIDP
6	Anthoniyammal	40/F	382/07	SLN	1Y3M	IV	Nil	Nil	N	-	Nil	68	17	0.9	12.1	6000	Nil	547	1039	ND	Not Sugg. of PN.
7	Paul Durai	33/M	82/06	SLE ZLN	3Y	IV	Nil	Nil	N	-	Nil	74	19	1.0	13.1	5600	Nil	15	672	ND	Not Sugg. of PN.
8	Jaganathan	41/M	103/09	SLE ATT	5M	IV	Nil	ATT	Y	3M	Y	93	14	1.0	11.3	4500	Nil	56	315	D	DSP
9	Kannu Pandiyan	39/M	9-Apr	SLN SLE	4Y	III	Nil	ATT 6M	Y	1Y	Y	84	19	1.2	8	4400	Nil	371	97	D	CIDP
10	Selvaraj	38/M	57/09	SLN	4M	III	Nil	Nil	N	-	Nil	66	16	1.0	10.8	8000	Nil	56	66	ND	Not Sugg. of PN.

11	Jesudoss	36/M	280/06	ZLE ZLN	2Y 9 M	III	Nil	Nil	N	-	Nil	78	33	0.9	14	3000	Nil	56	228	ND	Not Sugg. of PN.
12	Shanmugathai	23/F	203/08	SLN	1Y	I	Nil	Nil	N	-	Y	68	19	0.8	11.3	6000	Nil	286	722	D	DSP
13	Arumugam	38/M	95/08	SLN	1 Y 4 M	III	Nil	Nil	N	-	Nil	93	27	0.8	14	6500	Nil	150	160	ND	Not Sugg. of PN.
14	Murugan	30/M	381/07	ZLE ZLN	1 Y 10 M	I	Nil	Nil	Y	4M	Y	65	21	1	12.6	8600	Nil	834	259	D	DSP
15	Seetha	33/F	213/08	ZLN	1Y 4 M	IV	Nil	Nil	N	-	Nil	106	42	0.8	10.6	7200	Nil	NA	280	ND	Not Sugg. of PN.
16	Chandra	40/F	156/09	ZLN	2M	I	Nil	Nil	N	-	Nil	103	24	0.9	12.1	6500	Nil	NA	328	ND	Not Sugg. of PN.
17	Arumugam	40/M	251/09	ZLN	1M	I	Nil	Nil	Y	6M	Y	63	23	0.9	13	11000	Nil	322	156	D	DSP
18	Rathnaselvam	36/F	252/08	SLN ZLN	1Y	III	Nil	Nil	Y	1Y	Y	62	16	1.1	11.2	8000	Nil	37	263	D	DSP
19	Thangaraj	32/M	178/08	SLE ZLN	1Y 2M	III	Nil	Nil	N	-	Nil	91	24	1.2	10	4300	Ni	116	192	ND	Not Sugg. of PN.
20	Palavesam Balan	37/M	60/06	SLE ZLN	3Y6M	IV	Nil	Nil	Y	3M	Y	66	14	1.1	15	7000	Nil	76	948	D	DSP
21	Saravana Kumar	41/M	235/08	SLN	1Y	III	Nil	Nil	N	-	Nil	60	20	1.4	10	5000	Ni	34	218	ND	Not Sugg. of PN.
22	Balakrishnan	34/M	413/07	ZLE ZLN	1 Y 10 M	III	Nil	Nil	N	-	Nil	114	16.0	1.2	14.7	6800	Ni	432	253	ND	Not Sugg. of PN.
23	Pitchammal	23/F	137/07	SLN	2Y 5M	I	Nil	Nil	N	-	Nil	74	22	1.4	10.7	7600	Nil	58	637	ND	Not Sugg. of PN.

24	Mallika	30/F	23/07	SLE ZLN	2Y 6 M	III	Nil	Nil	N	-	Nil	96	30	1.1	11.8	6800	Nil	169	636	ND	Not Sugg. of PN.
25	Jayakodi	42/M	172/09	ZLE ATT	3M	III	Nil	ATT	Y	2M	Y	78	27	0.8	14.5	4400	Nil	NA	242	D	Distal sensory poly neuropathy
26	Mariyammal	42/F	154/06	ZLN	3M 6 M	III	Nil	Nil	N	-	Nil	63	16	0.6	8.4	4000	Nil	190	348	ND	Not Sugg. of PN.
27	Jecintha	33/F	14/07	ZLN	2Y 6 M	I	Nil	Nil	N	-	Nil	70	30	1.0	12	6500	Nil	339	411	D	Not Sugg. of PN.
28	Kandaraj	37/M	237/07	ZLN	2Y	III	Nil	Nil	N	-	Nil	80	40	1.6	13	8200	Nil	120	362	ND	Not Sugg. of PN.
29	Sumathy	24/F	744/06	SLN ZLN	3Y 6 M	I	Nil	Nil	N	-	Nil	69	19	0.9	12.5	8100	Nil	573	925	ND	Not Sugg. of PN.
30	Shanmugathai	46/F	334/08	SLE SLN	10M	III	Nil	Nil	N	-	Nil	83	27	0.9	15.9	7000	Nil	NA	395	ND	Not Sugg. of PN.
31	Shanmugaraj	30/M	197/07	SLE ZLN	2Y	III	Nil	Nil	Y	6M	Y	93	28	0.9	13	9000	Nil	46	512	D	DSP
32	Eswaran	36/M	97/09	ZLN	6M	III	Nil	Nil	Y	6M	Y	68	16	0.9	11.5	4700	Nil	442	232	D	DSP
33	Paul Pandi	41/M	279/06	SLN ZLN	3 Y	III	Nil	Nil	N	-	Nil	71	23	0.8	14	7000	Nil	187	639	ND	Not Sugg. of PN.
34	Mariappan	36/M	240/08	ZLN	1Y	III	Nil	Nil	N	-	Nil	106	24	1.0	13.5	6200	Nil	95	142	ND	Not Sugg. of PN.
35	Prema	28/F	331/08	SLE SLN	9M	IV	Nil	Nil	Y	1Y	Y	96	36	0.9	11.8	6300	Nil	-	206	D	DSP
36	Esakki	45/M	350/08	SLE SLN	10M	III	Nil	Nil	N	-	Nil	67	33	1.3	13	8100	Nil	39	200	ND	Not Sugg. of PN.

37	Indira	34/F	191/08	ZLE	1Y 3M	III	Nil	Nil	N	-	Nil	99	17	1.0	12.1	7400	Nil	397	471	ND	Not Sugg. of PN.
38	Samudrapandi	38/M	1423/06	ZLE ZLN	2Y 6M	III	Nil	Nil	N	-	Nil	88	38	1.1	14.2	7600	Nil	-	697	D	Distal sensory poly neuropathy
39	Balasaraswathi	28/F	163/08	SLN ZLN	1Y 3M	I	Nil	Nil	N	-	Nil	73	20	1.0	13.6	9500	Nil	360	654	D	Not Sugg. of PN.
40	Arumugam	28/M	440/07	ZLN	1Y 10M	III	Nil	Nil	N	-	Nil	65	18	0.8	12.8	5000	Nil	481	261	ND	Not Sugg. of PN.
41	Valarmathi	36/F	234/07	SLN	2Y 4M	III	Nil	Nil	Y	6M	Y	81	26	1.0	12.5	7800	Nil	310	628	D	DSP
42	Santhanamari	23/F	314/08	SLE ZLN	1Y	I	Nil	ATT	N	-	Nil	60	21	0.7	11.6	7500	Nil	94	420	ND	Not Sugg. of PN.
43	Thangaselvi	31/F	82/09	SLN	8M	III	Nil	Nil	Y	1Y	Y	78	34	1.0	11.2	4800	Nil	NA	576	D	CIDP
44	Radha	39/F	698/06	ZLN SLN	1Y 6M	I	Nil	Nil	Y	6M	Y	89	37	1.1	11.6	6200	Nil	NA	214	D	DSP
45	Ramakrishnan	54/M	389/07	SLN ZLN	2Y	III	Nil	Nil	Y	2M	Y	64	34	1.3	11.7	7400	Nil	49	145	D	MM
46	Uikattan	51/M	161/07	SLE SLN	2Y 4M	III	Nil	Nil	Y	6M	Y	109	15	0.9	11.2	6500	Nil	139	195	D	CIDP
47	Chellappa	32/M	63/06	ZLN	3Y 8 M	I	Nil	Nil	N	-	Nil	63	19	0.8	10	7100	Nil	161	282	ND	Not Sugg. of PN.
48	Indira	43/F	341/07	SLN	2Y 2 M	I	Nil	Nil	N	-	Nil	106	16	0.9	12.6	6200	Nil	NA	563	D	Not Sugg. of PN.

49	Petchiyammal	38/F	425/07	ZLE ZLN	2Y	I	Nil	Nil	N	-	Nil	65	38	0.9	11.7	6900	Nil	248	705	ND	Not Sugg. of PN
50	Rathinamathy	33./F	007/08	SLN	1Y 9M	I	Nil	Nil	N	-	Nil	76	20	0.9	9.8	6600	Nil	260	734	ND	Not sugg. of PN
51	Pitchammal	21/F	137/07	SLN	2Y 6M	I	Nil	Nil	Y	1Y	Y	74	22	1.1	10.7	7600	Nil	58	402	D	DSP
52	Selvin	35/M	337/06	SLN ZLN	4Y	III	Nil	Nil	N	-	Nil	83	36	1.1	12.1	6000	Nil	14	830	ND	Not sugg. of PN
53	Umaya Velayutham	41/M	138/08	SLN	1Y 6M	III	Nil	Nil	Y	2M	Y	101	20	1.3	14	7200	Nil	NA	268	D	DSP
54	Kalaiselvi	31/F	35/08	ZLN	1Y	II	Nil	Nil	Y	3M	Y	95	32	0.9	11.6	7600	Nil	NA	219	D	DSP
55	Mariappan	37/M	263/06	ZLE ZLN	3Y 3M	II	Nil	Nil	N	-	Nil	84	24	0.8	14	7400	Nil	168	700	ND	Not sugg. of PN
56	Shenbagam	52/F	249/09	ZLN	3M	I	NII	Nil	N	-	Y	98	40	1.3	10.8	6300	Nil	-	339	D	DSP
57	Manoharan	41/M	94/06	ZLE SLN	3Y 9 M	III	Nil	Nil	Y	6M	Y	93	37	1.1	13.6	7000	Nil	NA	424	D	CIDP
58	Parameshwari	25/F	21/07	ZLN	2Y 11M	I	Nil	Nil	N	-	Nil	87	34	1.1	13.5	7400	Nil	663	791	ND	Not sugg. of PN
59	Krishnammal	33/F	003/09	ZLN	9M	I	Nil	Nil	N	-	Nil	93	38	1.0	11.6	5800	Nil	NA	415	D	Not sugg. of PN
60	Therirajan	43/M	49/06	SLN ZLN	3Y 11M	IV	Nil	Nil	Y	6M	Y	86	42	1	11.9	6200	Nil	NA	256	D	DSP

DSP - Distal Symmetric Polyneuropathy, CIDP - Chronic Inflammatory Demyelinating Polyradiculoneuropathy, MM - Mononeuritis Multiplex, PN - Peripheral Neuropathy, Y-years, M-months, D-done, ND-not done, NA-

Dissertation on Peripheral Neuropathy in HIV Infected Patients

Master Chart (2)

No	ART Centre No	Patient's Name	MNC						SNC					
			Nerve	Latency (ms)	Amplitude (mv)	Duration (ms)	C. Velocity (m/s)	F. Wave Latency (ms)	Nerve	Latency (ms)	Amplitude (µv)	Duration (ms)	C. Velocity (m/s)	
1	387/07	Murugan	Right	3.9	2.4	21.0	47.9	Not	Right	2.5	15.0	4.6	47.2	
			Median	9.4	1.9	19.9		formed	Median					
			Left	3.2	6.5	15.3	50.1	Not	Left	2.3	13.8	3.2	47.2	
			Median	8.3	6.2	16.5		formed	Median					
			Right	3.0	6.7	8.5	33.0	Not	Both surals Not recordable					
			Tibial	12.7	6.4	8.3		formed						
			Left	4.5	1.7	10.2	26.8	Not						
			Tibial	17.1	0.4	7.3		formed						
2	147/09	Mariappan	Right	3.0	4.4	14.1	54.6	Not	Right	2.3	15.2	3.2	57.8	
			Median	7.6	5.1	14.5		formed	Median					
			Left	3.7	5.7	4.9	57.2	Not	Left	2.0	12.9	2.9	61.2	
			Ulnar	8.0	4.9	5.0		formed	Median					
			Right	4.5	14.0	9.0	40.3	Not	Both surals not recordable					
			Tibial	12.9	17.7	9.1		formed						
			Left	4.8	4.2	9.0	46.1	Not						
			Peroneal	12.6	3.3	10.7		formed						
3	35/09	Kathirvel	Right	3.0	5.7	11.4	57.1	Not	Right	2.4	7.5	2.3	50.4	
			Median	7.4	4.8	10.7		formed	Median					
			Left	2.5	6.9	13.9	51.0	Not	Left	1.9	8.6	2.9	56.1	
			Ulnar	7.4	6.9	13.4		formed	Ulnar					
			Right	3.3	6.0	9.7	46.1	Not	Right	5.9	0.9	1.0	25.3	
			Peroneal	11.4	7.0	11.8		formed	Sural					
			Left	2.8	10.9	7.5	42.5	Not	Left	5.8	31.0	3.1	18.7	
			Tibial	11.9	9.0	7.7		formed	Sup.Peroneal					
4	103/09	Jega - Nathan	Right	4.0	7.8	14.4	56.4	32.1	Right	2.4	22.0	3.2	52.9	
			Ulnar	8.8	7.4	18.2			Median					
			Left	3.5	7.8	15.8	57.6	Not	Left	2.0	7.5	3.7	53.9	
			Median	7.7	7.2	17.1		formed	Ulnar					
			Right	4.5	8.5	8.9	28.0	62.0	Right sural and Left Superficial Peroneal not recordable					
			Tibial	16.3	6.9	10.5								
			Left	3.9	3.0	16.2	33.0	39.0						
			Peroneal	13.5	2.5	18.0								

5	4/09.	Kannu - Pandiyan	Right Median	2.9 7.5	13.8 13.4	17.3 17.7	52.4	Not formed	Right Median	3.0	13.5	2.8	37.2
			Left Median	2.8 7.3	17.5 16.5	13.4 13.8	53.6	Not formed	Left Median	2.6	16.6	2.8	42.0
			Right Peroneal	4.1 17.1	2.0 1.0	8.0 4.8	24.6	Not formed	left Sural	6.2	5.9	0.3	24.3
			Left Tibial	4.3 14.7	8.7 6.5	8.9 9.9	34.6	Not formed	Right Sural	NR			
6	203/08.	Shanmuga - Thai	Right Median	2.5 6.5	11.1 10.8	13.1 13.5	55.6	24.5	Right Median	2.4	18.6	3.8	45.5
			Left Ulnar	1.7 5.3	10.0 9.9	12.9 12.2	56.7	26.3	Left Ulnar	1.6	5.4	2.1	63.3
			Right Peroneal	1.9 8.9	5.8 3.7	7.2 6.2	46.6	Not formed	Right Sural	NR			
			Right Tibial	3.1 11.3	14.2 11.6	6.8 7.7	49.2	Not formed	Left Sural	NR			
			Left Peroneal	2.0 8.8	2.1 1.6	8.2 9.0	48.7	Not formed					
			Left Tibial	3.1 10.9	15.3 11.7	8.9 9.8	43.5	Not formed					
7	381/07	Murugan	Right Ulnar	2.4 7.2	6.2 5.0	13.9 14.5	50.1	29.9	Right Median	2.2	27.7	2.6	50.7
			Left Median	3.0 7.1	10.0 10.2	14.7 13.3	59.1	Not formed	Right Ulnar	1.9	14.5	2.4	48.4
			Left Ulnar	4.3 8.8	11.2 8.0	7.0 9.6	55.8	30.7	Left Median	2.0	15.2	2.3	56.1
			Right Peroneal	2.7 10.5	1.7 1.3	14.1 16.8	46.1	Not formed	Left Ulnar	2.0	5.4	3.8	49.0
			Right Tibial	3.8 12.5	22.9 18.4	8.1 9.4	42.3	47.9	Right Sural	3.2	4.0	2.0	44.2
			Left Peroneal	2.9 10.4	6.0 5.6	13.1 14.6	42.7	Not formed	Left Sural	2.8	4.2	2.0	53.8
8	251/09	Arumugam	Right Median	2.5 5.9	11.6 11.3	11.3 10.9	58.1	26.2	Right Median	2.2	11.6	3.0	50.6
			Left Ulnar	2.4 6.0	8.2 12.2	12.3 12.9	68.7	29.8	Left Ulnar	2.0	8.2	4.1	49.5
			Right Peroneal	2.5 11.5	6.3 5.2	11.7 12.8	40.2	Not formed	Left Sural	6.3	4.7	1.5	23.7
			Right Tibial	3.3 13.3	9.3 11.1	11.8 11.8	37.0	56.8	Right Sural	NR			
			Left Peroneal	4.4 12.7	2.2 1.7	15.9 15.3	40.8	Not formed					
			Left	4.5	9.2	8.8	36.4	58.1					

			Tibial	15.2	10.6	9.4								

9	252/08	Rathina - Selvam	Right Ulnar	3.3 7.6	12.0 11.0	9.2 9.1	53.9	28.9	Right Median	2.5	10.0	2.5	43.3
			Left Median	2.6 7.3	16.6 13.9	9.5 10.4	51.2	27.1	Left Ulnar	2.8	32.4	3.3	35.8
			Right Peroneal	3.2 12.0	5.2 4.5	9.7 10.3	45.7	Not formed	Right Sural	3.9	1.3	0.3	38.3
			Left Tibial	3.1 12.6	17.5 14.4	8.3 8.0	39.0	Not formed	Left Sural	NR			
10	60/06	Palavesam Balan	Right Median	2.2 6.2	10.2 10.2	16.2 16.4	55.6	29.2	Right Median	2.1	22.7	3.8	52.3
			Left Ulnar	2.4 6.0	8.6 8.6	14.3 16.6	63.2	27.8	Left Ulnar	1.5	10.7	3.1	66.7
			Right Tibial	4.1 14.5	3.0 7.9	10.4 10.8	37.4	Not formed	Left Sural	4.1	1.8	2.0	36.4
			Left Peroneal	Not Stimulatable					Right Sural	NR			
			Right Peroneal	Not Stimulatable									
			Left Tibial	4.3 15.3	12.5 12.3	9.3 9.2	37.2	Not formed					
11	172/09	Jayakodi	Right Median	3.7 8.1	12.3 11.9	16.4 18.1	51.5	29.6	Right Median	2.6	4.6	2.5	42.0
			Left Ulnar	2.7 7.3	8.8 8.0	12.9 13.9	56.8	30.6	Left Ulnar	2.0	10.5	3.4	51.0
			Right Tibial	4.2 12.6	4.0 4.2	9.2 12.3	43.8	52.0	Right Sural	NR			
			Left Tibial	3.4 11.2	12.6 11.2	9.8 10.2	42.3	51.6	Left Sural	NR			
12	14/07	Jecintha	Right Median	2.4 6.0	18.2 17.4	11.2 11.5	57.7	24.8	Right Median	1.9	10.3	2.7	57.3
			Left Ulnar	3.3 6.9	6.6 6.3	10.6 11.1	62.0	24.8	Left Ulnar	1.4	3.1	2.6	70.4
			Right Peroneal	2.5 8.8	8.1 7.9	9.2 10.4	52.8	Not formed	Right Sural	4.3	7.8	3.9	39.2
			Left Tibial	2.5 10.3	2.5 4.3	8.5 8.1	44.8	53.4	Left Sural	4.0	8.2	3.8	40.4
13	197/07	Shanmuga-Raj	Right Median	3.7 8.7	6.5 6.2	14.9 16.2	52.0	Not formed	Right Median	2.5	13.2	3.5	48.0
			Left Ulnar	3.3 8.5	9.3 7.8	11.9 10.8	49.9	30.7	Left Ulnar	1.9	12.9	2.9	53.2
			Right Peroneal	Not Elicitable					Right Sural	NR			
			Left	Not Elicitable					Left	NR			


Tibial
Sural

14	97/09	Eswaran	Right	3.3	7.4	12.7	50.2	27.8	Right	2.6	9.1	4.9	42.6
			Median	7.7	6.4	13.3			Median				
			Left	3.0	6.7	14.0	57.6	28.3	Right	2.0	11.3	3.4	49.0
			Ulnar	7.2	7.4	14.3			Ulnar				
			Right	6.6	1.3	17.7	35.4	Not	Left	2.0	29.3	2.9	55.0
			Peroneal	15.3	0.8	13.4		formed	Median				
			Left	5.6	8.8	10.7	40.1	50.8	Left	4.9	1.2	1.4	30.2
			Tibial	13.8	8.0	10.7			Sural				
									Right	3.8	27.3	2.9	39.6
									Sural				
15	331/08	Prema	Right	2.7	14.4	19.8	50.2	30.8	Right	2.3	15.0	2.8	47.2
			Median	7.3	13.6	19.0			Median				
			Left	2.6	7.1	9.6	46.1	31.2	Left	2.0	7.4	3.8	53.9
			Ulnar	8.0	7.1	8.1			Ulnar				
			Right	3.1	2.5	10.9	35.8	Not	Right	NR			
			Peroneal	11.8	2.0	10.0		formed	Sural				
			Left	3.3	14.4	10.4	36.6	Not	Left	NR			
			Tibial	12.1	11.4	10.6		formed	Sural				
16	1423/06	Samudra	Right	2.2	12.9	13.4	55.6	25.2	Right	2.2	14.4	2.5	49.8
		Pandi	Median	6.2	12.6	13.9			Median				
			Left	4.3	8.2	11.6	60.0	30.9	Left	2.0	8.8	4.0	50.0
			Ulnar	8.4	12.1	10.5			Ulnar				
			Left	3.7	15.7	8.0	45.9	45.4	Right	NR			
			Tibial	10.8	13.0	9.2			Sural				
									Left	NR			
									Sural				
17	163/08	Bala	Right	2.1	9.9	12.1	76.2	25.4	Left	2.5	19.9	3.9	43.3
		Saraswathy	Ulnar	5.1	9.4	12.2			Median				
			Left	2.4	12.3	11.4	58.3	23.3	Right	1.5	6.7	2.2	66.7
			Median	5.8	11.9	11.0			Ulnar				
			Right	2.3	3.6	7.7	51.2	Not	Left	3.1	6.5	1.7	48.1
			Peroneal	8.5	5.2	9.0		formed	Sural				
			Left	3.7	21.0	8.9	43.3	50.5	Right	3.8	6.3	1.9	46.3
			Tibial	11.0	22.2	8.9			Sural				
18	234/07	Valar-	Right	3.7	11.6	12.6	65.0	27.5	Right	2.9	7.4	0.8	38.2
		mathy	Median	7.2	10.4	13.7			Median				
			Left	1.9	4.5	10.6	52.6	26.7	Left	1.7	6.3	3.3	59.9
			Ulnar	6.3	3.0	10.5			Ulnar				
			Right	2.9	4.2	10.4	42.0	48.1	Right	NR			
			Peroneal	11.3	4.3	12.7			Sural				
			Left	3.2	6.7	8.3	35.3	52.6	Left	NR			
			Tibial	12.3	6.4	8.8			Sural				

19	82/09	Thanga-selvi	Right Median	2.5	13.6	12.3	52.5	29.5	Right Median	2.4	8.7	3.7	45.5
			Left Ulnar	2.1	8.5	11.3	54.5	Not formed	Left Ulnar	2.0	9.3	2.0	51.0
			Right Peroneal	2.0	6.6	10.2	38.6	Not formed	Right Sural	NR			
			Left Tibial	3.7	12.8	7.1	34.9	Not formed	Left Sural	NR			
20	698/06	Radha	Right Median	3.1	10.2	15.8	52.5	25.6	Right Median	2.4	22.6	3.5	45.5
			Left Ulnar	2.3	11.2	14.4	53.9	27.7	Left Ulnar	2.0	7.2	2.4	51.0
			Right Peroneal	2.4	4.3	14.5	40.5	Not formed	Right Sural	3.4	3.8	3.5	44.4
			Left Tibial	4.6	13.4	9.4	35.4	53.3	Left Sural	NR			
21	389/07	Rama-Krishnan	Right Median	3.3	10.7	11.4	46.9	29.8	Right Median	2.5	9.6	3.5	48.9
			Left Ulnar	4.4	4.3	10.0	51.1	30.0	Left Ulnar	3.0	7.6	2.0	33.8
			Right Peroneal	2.6	3.4	9.7	40.2	53	Left Sural	3.8	0.7	0.8	40.0
			Left Tibial	3.0	7.0	6.8	37.3	Not formed	Right Sural	3.2	6.1	2.8	47.3
22	161/07	Uikattan	Right Ulnar	4.5	8.6	8.7	54.2	29.7	Right Ulnar	1.8	12.2	3.0	54.6
			Left Median	2.9	9.5	10.6	43.7	Not formed	Left Median	2.3	16.9	2.6	48.9
			Right Peroneal	2.4	2.2	5.7	38.0	Not formed	Left Sural	3.8	5.2	2.7	39.6
			Left Tibial	2.9	7.9	9.2	37.1	58.8	Right Sural	NR			
23	341/07	Indira	Right Median	2.7	11.3	14.4	50.4	29.4	Right Median	2.4	24.4	2.8	45.5
			Left Median	3.7	8.2	10.6	50.3	27.3	Left Ulnar	1.8	25.4	2.1	57.1
			Right Peroneal	3.1	6.2	11.4	43.2	47.9	Right Sural	4.0	8.0	4.0	37.5
			Left Tibial	5.6	5.7	7.1	50.6	49.1	Left Sural	5.4	3.7	2.8	37.1

24	137/07	Pitchammal	Right Median	3.4 7.6	14.3 14.1	13.9 14.3	50.5	27.3	Right Median	2.8	9.3	2.9	40.0
			Left Ulnar	4.8 9.0	5.0 5.1	4.8 4.9	52.8	26.7	Left Ulnar	1.7	14.9	2.5	58.5
			Right Peroneal	2.8 11.0	6.3 6.7	12.1 12.1	40.1	Not formed	Right Sural	NR			
			Left Tibial	4.1 11.5	15.0 18.2	11.0 12.7	40.5	44.5	Left Sural	NR			
25	138/08	Umaya-velayudham	Right Median	3.0 7.6	12.8 13.3	11.6 11.6	48.0	29.8	Right Median	2.3	6.9	2.6	48.0
			Left Ulnar	4.3 8.9	4.1 3.8	5.6 5.4	48.0	27.6	Left Ulnar	2.1	11.1	2.5	47.2
			Right Peroneal	2.1 9.9	5.2 4.2	9.9 11.2	38.4	Not formed	Left Sural	5.7	13.8	1.9	26.5
			Left Tibial	3.4 11.8	15.5 13.0	9.1 10.0	38.4	49.8	Right Sural	NR			
26	35/08	Kalai-selvi	Right Median	2.5 6.4	11.4 10.2	14.4 13.9	54.6	Not formed	Right Median	2.2	6.1	2.3	50.7
			Left Ulnar	5.2 9.0	13.6 13.0	10.0 10.0	56.0	27.4	Left Ulnar	1.7	4.5	3.7	59.9
			Right Peroneal	2.2 9.5	7.2 5.5	10.7 10.4	41.1	Not formed	Right Sural	NR			
			Left Tibial	3.4 10.4	8.2 7.9	11.5 12.1	37.2	Not formed	Left Sural	NR			
27	249/09	Shenbagam	Right Median	2.7 6.8	13.2 12.8	12.3 12.8	51.7	31.2	Right Median	2.2	16.4	3.6	50.1
			Left Ulnar	2.7 6.9	3.3 3.2	10.4 9.9	50.4	29.8	Left Ulnar	2.1	7.5	2.5	48.1
			Right Peroneal	2.8 10.4	7.4 7.8	10.0 9.7	40.7	52.5	Right Sural	NR			
			Left Tibial	3.9 12.4	10.4 9.5	8.9 9.8	32.8	54.5	Left Sural	NR			
28	94/06	Manoharan	Right Median	2.7 7.3	15.6 14.5	19.8 19.0	50.2	30.6	Right Median	2.3	8.1	3.5	48.0
			Left Ulnar	3.1 7.8	7.8 8.0	12.2 12.4	51.2	32.1	Left Ulnar	2.8	7.3	4.3	35.8
			Right Peroneal	2.0 11.2	5.6 4.3	14.4 12.3	36.0	Not formed	Right Sural	NR			
			Left Tibial	6.4 15.5	6.8 4.9	6.6 7.6	34.9	Not formed	Left Sural	NR			

29	003/09	Krish - nammal	Right Median	2.4	13.7	13.7	54.2	24.3	Right Median	1.9	28.8	3.1	58.5
			Left Ulnar	2.1	10.0	14.6	63.0	26.4	Left Ulnar	1.5	14.0	2.6	66.7
				5.7	10.4	16.9							
			Right Tibial	3.8	18.6	8.5	42.5	47.8	Right Sural	3.8	8.0	4.1	38.7
				11.0	15.7	9.7							
			Left Peroneal	5.3	2.5	8.2	49.4	47.8	Left Sural	2.8	3.6	2.1	53.8
				12.4	1.8	9.9							
30	49/06	Therirajan	Right Median	2.8	11.9	13.7	53.6	Not formed	Right Median	2.1	16.7	2.6	51.9
				7.3	11.5	13.8							
			Left Ulnar	2.6	2.7	10.6	56.1	Not formed	Left Ulnar	1.9	12.5	2.6	52.1
				6.9	1.8	11.5							
			Right Tibial	4.3	6.6	9.5	34.6	Not formed	Right Sural	NR			
				14.7	5.0	10.6							
			Left Peroneal	4.1	3.9	11.0	48.0	Not formed	Left Sural	NR			
				10.5	2.1	13.1							

NR - Not Recordable

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