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A PROSPECTIVE OBSERVATIONAL STUDY ON THE PRESCRIBING PATTERN AND OF QUALITY OF LIFE IN PATIENTS WITH PERIPHERAL NEUROPATHIC PAIN

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ABSTRACT

Peripheral neuropathic pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. A person's perception of pain is influenced by their emotional state, the circumstances around how they first experienced the pain and whether they believed it to be a hazardous signal. The most commonly prescribed drugs for neuropathic pain include Pregabalin, Gabapentin and Methylcobalamine along with other drugs for co-morbid conditions. The aim of the study is to evaluate and analyse the prescribing pattern and quality of life in patient with peripheral neuropathic pain. The objectives are To analyse the prescribing pattern of drugs in peripheral neuropathic pain and To assess the improvement in quality of life of patients with peripheral neuropathy. The Prospective observational study was conducted in 77 patients who are diagnosed with Peripheral neuropathic pain in the neurology department. The prescribing pattern of drugs used in peripheral neuropathy was analysed from the prescription. The improvement in the quality of life of the patients were assesed by using NEURO – QOL scale after providing proper patient counselling. The most commonly prescribed drugs for neuropathic pain were found to be Pregabalin, Gabapentin, Lacosamide and Methylcobalamine. A significant increase in quality of life was found in patients after treatment and patient counselling. It was concluded that anti-convulsant like Pregabalin, Gabapentin and Lacosamide along with Methylcobalamine and other drugs for co- morbid conditions are prescribed for peripheral neuropathic pain. There is significant in the QOL scoring in patients after treatment and patient counselling.

KEYWORDS: Neuropathic Pain, Neuro QOL, Diabetics, Pregabalin, Gabapentin, Lacosamide.

1. INTRODUCTION

Peripheral neuropathic pain is a condition that affects and alters the mood and quality of life of patients. Quality of life is defined as "individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concern".[1] Neuro-QoL is a measurement system that evaluates and monitors the physical, mental and social effects experienced by adults and children living with neurological condition.[2] The Leeds assessment of neurological signs and symptoms scale is used to distinguish whether the pain experienced is originated due to neuronal damage or any other reasons. A score of above 12 in the Leeds assessment of neurological signs and symptoms scale shows that the pain is due to neurological causes.[3] A person's perception of pain is influenced by their emotional state, the circumstances around how they first experienced the pain and whether they believed it to be a hazardous signal. It is difficult to quantify the intensity of pain.[4]

Neuropathic pain is the injury to neuronal tissue in the central nervous system or peripheral nervous system initiates neuropathic pain. Neuropathy is a disturbance of function or a change in one or several nerves. About 30% of all neuropathic pain happens because of diabetes but other diseases like alcoholism and shingles can cause neuropathic pain. Neuropathic pain can be divided in to two Peripheral neuropathic pain and Central neuropathic pain.

Central neuropathic pain is associated with central nervous system lesions, which includes spinal cord injury, head trauma, stroke, multiple sclerosis whereas peripheral neuropathic pain occurs when damage occurs to nerves outside brain and spinal cord. It includes trigeminal neuralgia, nerve lesion, painful neuropathy, postherpetic neuralgia.[5] The potential causes of neuropathic pain include diabetes, vitamin B deficiency, hypertension, alcoholism, smoking and obesity among which diabetes is most leading cause. Patients with uncontrolled diabetes can easily end up in neuronal damage leading to severe neuropathic pain. Patients with peripheral neuropathic pain are presented with symptoms like tingling sensation, numbness, weakness, burning/stabbing pain, paraesthesia, loss of balance, nocturnal aggravation.[6]

1.1NEUROPATHIC PAIN

According to International Association for the Study of Pain(IASP)" Pain" is a distressing sensory and emotional experience connected to real or potential tissue damage, or one that is portrayed as such damage.[7] There are many pathophysiologic processes and interpretation of pain, which can vary greatly in severity, quality and duration.[8] Injury to neural tissue in Central Nervous System (CNS) or Peripheral Nervous System (PNS) initiates or causes neuropathic pain.[9] Neuropathy is a disturbance of function or a change in one or several nerves. Patients with neuropathic pain frequently express discomfort from stimuli that are not typically harmful, such as a breeze or light touch, in addition to spontaneous pain.[10] Peripheral neuropathy can be subdivided into 3 types, mononeuropathy, mononeuropathy multiplex and polyneuropathy, based on the involvement of single nerve, multiple single nerves, or many nerves respectively, in a symmetric length-dependent fashion.[11]

1.1 CLASSIFICATION

Peripheral neuropathy may be classified according to the number and distribution of nerves affected (mononeuropathy, mononeuritis multiplex, or polyneuropathy), the type of nerve fibre predominantly affected (motor, sensory, autonomic), or the process affecting the nerves; e.g., inflammation (neuritis), compression (compression neuropathy), chemotherapy (chemotherapy-induced neuropathy). The affected nerves are found in an EMG (electromyography) / NCS (nerve conduction study) test and the classification is applied upon completion of the exam.[13]

1.1.1 MONONEUROPATHY

Mononeuropathy is a type of neuropathy that only affects a single nerve. Diagnostically, it is important to distinguish it from polyneuropathy because when a single nerve is affected, it is more likely to be due to localized trauma or infection. The most common cause of mononeuropathy is physical compression of the nerve, known compression neuropathy. Carpel tunnel syndrome and axillary nerve palsy are examples. Direct injury to a nerve, interruption of its blood supply resulting in(ischemia), or inflammation also may cause mononeuropathy.[14]

1.1.2 POLYNEUROPATHY

"*Polyneuropathy*" is a pattern of nerve damage that is quite different from mononeuropathy, often more serious and affecting more areas of the body. The term "peripheral neuropathy" sometimes is used loosely to refer to polyneuropathy. In cases of polyneuropathy, many nerve cells in various parts of the body are affected, without regard to the nerve through which they pass; not all nerve cells are affected in any particular case. In distal axonopathy, one common pattern is that the cell bodies of neurons remain intact, but the axons are affected in proportion to their length; the longest axons are the most affected.

Diabetic neuropathy is the most common cause of this pattern. In demyelinating polyneuropathies, the myelin sheath around axons is damaged, which affects the ability of the axons to conduct electrical impulses. The third and least common pattern affects the cell bodies of neurons directly. This affects the sensory neurons (knownas *sensory neuronopathy* or *dorsal root ganglionopathy*).[15,16] Polyneuropathies usually are caused by processes that affect the body as a whole. Diabetes and impaired glucose tolerance are the most common causes. Hyperglycaemia-induced formation of advanced glycation end products (AGEs) is related to diabetic neuropathy.[17] Other causes relate to the particular type of polyneuropathy, and there are many different causes of each type, including inflammatory diseases such as Lyme disease, vitamin deficiencies, blood disorders, and toxins (including alcohol and certain prescribed drugs).

1.1.3 MONONEURITIS MULTIPLEX

Mononeuritis multiplex, occasionally termed polyneuritis multiplex, is simultaneous or sequential involvement of individual non-contiguous nerve trunks,[18] either partially or completely, evolving over days to years and typically presenting with acute or subacute loss of sensory and motor function of individual nerves. The pattern of involvement is asymmetric. However, as the disease progresses, deficit(s) becomes more confluent and symmetrical, making it difficult to differentiate from polyneuropathy.

Mononeuritis multiplex is sometimes associated with a deep, aching pain that is worse at night and frequently in

the lower back, hip, or leg. In people with diabetes mellitus, mononeuritis multiplex typically is encountered as acute, unilateral, and severe thigh pain followed by anterior muscle weakness and loss of knee reflex.

1.1.4 AUTONOMIC NEUROPATHY

Autonomic neuropathy is a form of polyneuropathy that affects the non-voluntary, non-sensory nervous system (i.e., the autonomic nervous system), affecting mostly the internal organs such as the bladder muscles, the cardiovascular system, the digestive tract, and the genital organs. These nerves are not under a person's conscious control and function automatically. Autonomic nerve fibres form large collections in the thorax, abdomen, and pelvis outside the spinal cord. They have connections with the spinal cord and ultimately the brain. However, most commonly autonomic neuropathy is seen in persons with long-standing diabetes mellitus type 1 and 2. In most but not all cases, autonomic neuropathy occurs alongside with other forms of neuropathy, such as sensory neuropathy.[19]

Autonomic neuropathy is one cause of malfunction of the autonomic nervous system, but not the only one; some conditions affecting the brain or spinal cord also may cause autonomic dysfunction, such as multiple system atrophy, and therefore, may cause similar symptoms to autonomic neuropathy.

1.1.5 NEURITIS

Neuritis is a general term for inflammation of a nerve or the general inflammation of the peripheral nervous system. Symptoms depend on the nerves involved, but may include pain, paresthesia, paresis (weakness), hypoesthesia (numbness), anesthesia, paralysis, wasting, and disappearance of the reflexes. Causes of neuritis include:

- Physical injury
- Infection
- Diphtheria
- Herpes zoster (shingles)
- Leprosy
- Lyme disease
- Chemical injury such as chemotherapy
- Radiation therapy

Types of neuritis include

- Brachial neuritis
- Cranial neuritis such as Bell's palsy
- Optic neuritis

1.2 TYPES OF NEURONAL PAIN[10]

Types of Neuronal Pain	Causes
Trigeminal Pain	Compression of trigeminal or its branches
Post herpetic Pain	Shingles
Complex regional pain syndrome	Trauma
Diabetic neuropathy	Persistent Hyperglycemia
Central Pain	Trauma to spinal cord
Phantom Pain	Amputation

1.2.1 TRIGEMINAL NEURALGIA

Trigeminal neuralgia is a chronic neuropathic pain disorder affecting one or more branches of the trigeminal nerve. It is characterized by brief pain attacks described as sharp, stabbing, or electric shock like. Trigeminal neuralgia is further classified in to classical, secondary or idiopathic, according to etiology.[20]

1.2.2 POST HERPETIC PAIN

Post herpetic neuralgia is usually a constant or intermittent burning, stabbing, or sharp, shooting pain with hyperalgesia, persisting beyond the healing of herpetic skin lesions more than 4 weeks after the rash onset. Another proposed definition of herpes related pain is subacute herpetic neuralgia 30- 90 days from herpes zoster and post herpetic neuralgia if the pain persists beyond 3 months.[22]

1.2.3 COMPLEX REGIONAL PAIN SYNDROME

Complex regional pain syndrome is a chronic and painful condition. It is usually triggered by a traumatic event of soft tissues involving the nervous tissue. The pain is associated with changes in the autonomic nervous system and has a distal predominance.[24]

1.2.4 DIABETIC NEUROPATHY

Diabetic neuropathy is a well-known microvascular complication of type 2 diabetes mellitus attributed to chronic hyperglycemia, and is defined as presence of peripheral nerve dysfunction in diabetes after exclusion of other causes.[25]

1.2.5 CENTRAL PAIN

Central neuropathic pain is caused by a lesion or disease of the central somatosensory pathway in the spinal cord. This condition can also be derived from the chronic pain after spinal cord injury, referring to patients who have neuropathic component as well.[26]

1.2.6 PHANTOM PAIN

Phantom limb pain refers to painful sensation in an amputated or denervated part of the body. It is a phenomenon commonly observed in orthopedic rehabilitation units that can have detrimental effects on

patient functioning

1.3 EPIDEMIOLOGY

Peripheral neuropathy is a group of heterogeneous disorder with a wide etiological spectrum and presents to physicians and neurologists in the community frequently.[27]

- The prevalence of peripheral neuropathy varies from 5 to 2400 per 1000 population in different community studies.
- Diabetes mellitus (DM) is a common cause of neuropathy worldwide.
- Prevalence of peripheral neuropathy in diabetic patients ranges from 10.5% to 32.2% and up to 50% patients will eventually develop neuropathy during the course of their disease.
- According to an Indian study it was estimated that the incidence of polyneuropathy from medications or toxins to be 2% to 4%.

1.4 ETIOLOGY

Possible etiologies of peripheral neuropathies.[28,29]

Endocrine disease
- Hypothyroidism
- Diabetes Mellitus
- Nutritional Diseases
- Alcoholism
- Vitamin b12 deficiency
- Thiamine deficiency
- Crohn's disease

Connective tissue diseases
- Rheumatoid arthritis
- Systemic Lupus erythematous
- Polyarteritis nodosa

Infectious diseases
- AIDS
- Lyme disease
- Hereditary disesases
- Charcot – Marie -Tooth syndrome
- Freidreich's ataxia
- Other sensory neuropathies

Metal neuropathy
- Mercury
- Thalium
- Chronic arsenic intoxication
- Medications
- Isoniazid
- Hydralazine
- Metronidazole
- Lithium
- Alpha interferon
- Dapson
- Phenytoin
- Amiodarone
- Pyridoxine

Toxic neuropathy
- Acrylamide
- Carbon disulphide
- Ethylene oxide
- Carbon monoxide

Neuropathies caused by drugs[30]

Antineoplastic Agents
- Cisplatin
- Taxanes
- Vincristine

Antimicrobial Agents
- Chloroquine
- Dapsone
- Isoniazid

Antiviral agents
- Lamivudine
- Stavudine

1.5 PATHOPHYSIOLOGY

Knowledge of the cellular and molecular mechanism of neuropathic pain has advanced with development of various experimental models of nerve injury.[31]

Two kinds of pathophysiological process occur in neuropathies.

- First, the nerve cell body and axon may be primarily affected leading to axonal degeneration. The pathophysiological appearances resemble those of Wallerian degeneration which follows a crush injury to nerve.
- Secondly, the Schwann cell may be affected causing demyelination without involvement of the axon. This process is termed as segmental demyelination.
- In chronic neuropathies there is evidence of partial regeneration of nerves.
- Regeneration after nerve injury results in the formation of neuromas and sprouting of new nerve projections among uninjured neighboring neurons
- Collateral sprouting leads to altered sensory properties that may be realized as expanded receptive fields.
- After axonal degeneration, regeneration is slow and incomplete, after demyelination, recovery, if it occurs is rapid and more complete.
- Axonal degeneration occurs after a focal lesion in the nerve other than trauma or after general insults.
- It is often difficult to distinguish between a process affecting the terminal part of longest fibers and a process affecting only the neurons with the longest fibers.
- Sometimes both the axon and neuron are affected.
- A feature of recurrent segmental demyelinating neuropathies is the development of hypertrophic neuropathy.
- Each episode of the demyelination causes further division of the Schwann cells the new cells being unable to find a place on the axon, so leading to

axon bulb formation and sometimes clinically palpable thickening of the nerves. This occurs in the steroid-responsive recurrent polyneuropathy and also in hereditary sensory neuropathy.
- The demyelinating process in diabetes has been interpreted as either the result of primary progressive axonal atrophy of direct damage to schwann cells secondary to ischemia or metabolic disturbances.
- Nerve fiber loss in diabetic neuropathy is distributed multifocally within individual.
- Fiber depletion increases from proximal to distal in the nerves.
- Sustained painful stimuli results in spinal sensitization, which is defined as heightened sensitivity of spinal neurons, reduced activated thresholds and enhanced responsiveness to synaptic inputs.

1.6 RISK FACTORS[32]
- Age
- Duration of Diabetes mellitus (DM)
- Smoking
- Hypertension
- Microvascular complication
- Macrovascular complication
- Glycated hemoglobin
- Dyslipidemia
- Alcoholism
- Macroalbuminuria
- Obesity

1.7 CLINICAL PRESENTATION
- Gradual beginning of tingling, prickling, or numbness in your hands or feet that may go up into your legs or arms.[33,34]
- Pain that is throbbing, jabbing, or sharp.
- A high threshold for touch.
- Pain that occurs during actions that shouldn't cause it, such foot pain when placing weight on it or when it's covered by a blanket.
- Falling and poor coordination.

1.8 DIAGNOSIS[36]
- TAKING A THROUGH MEDICAL HISTORY: The doctor will take complete medical history of the patient, including symptoms, lifestyle, toxin exposure, Habits and any family histories of neurological (nervous system) problems.
- **NEUROLOGICAL EXAM:** Examination of body posture and coordination in addition to tendon reflexes, muscle strength, and muscle tone.
- **BLOOD TEST:** These can find signs of illness that can cause peripheral neuropathy, such as vitamin deficiencies, diabetes, aberrant immunological function, and others.
- **IMAGING EXAMS:** CT or MRI scans can check for tumors, herniated discs, pinched (compressed) nerves, blood vessels abnormalities, and other condition affecting the bones and blood vessels.[37]
- **TEST OF NERVE FUNCTION:** Muscles electrical activity is captured by electromyograph (EMG), which can identify nerve damage. To record electrical activity as the muscle contracts, a tiny needle (electrode)is placed into the muscle. A nerve conduction test measures how fast an electrical impulse moves through your nerve. This test help find out if you have a health condition that has damaged your muscles or nerves or how they work together. At the same time your doctor or am EMG technician obtains an electromyogram, he or she typically performs a nerve conduction study. Flat electrodes are placed on the skin and a low electric current stimulates the nerves. The doctor will record your nerves responses to the electric current.[38]
- **TEST OF OTHER NERVE FUNCTIONS:** Some of them could be an autonomic reflex screen, which documents the functioning of the autonomic nerve fibers, a sweat test, which gauges your body's sweat production, and sensory test, which document your perception of tough, vibration, cooling, and heat.
- **BIOPSY OF A NERVE:** In order to check for anomalies, a tiny section of nerve, typically a sensory nerve, may be removed.[39]
- **SKIN BIOPSIES:** In order to check for loss in nerve endings, your doctor may remove a little amount of skin.[40]

DIAGNOSTIC CRITERIA AND GRADING[41]
It appears important that the diagnostic criteria are clearly stated by various investigators. Most neurologists put more weight on signs than symptoms and require the presence of at least one bilateral sign in addition to symptoms. In the absence of symptoms, two or more signs may be required, such as stocking pattern of hypoesthesia or decreased vibratory sensation in the feet, together with loss of ankle or weakness of toe dorsiflexors. Since the diagnostic significance increases with the number and extent of abnormalities, it is reasonable to interpret the number of abnormal tests and degree of impairment of each function as overall measure of nerve dysfunction.

1.9 MANAGEMENT
PHARMACOLOGOCAL TREATMENT
Therapeutic agents with greater efficacy and safety are necessary because traditional analgesics like non-steroidal anti-inflammatory medication (NSAIDs) and opioid agonists (e.g.; morphine) are in effective in some pain disorders and have issues of side effects.[42,43] The secretion and metabolism of neurotransmitters like serotonin, norepinephrine, neurokinin, GABA, and glutamate, as well as their receptors like NMDA, are significant targets. Studies on pain treatment are increasingly involving ion channels, TRP and P2 receptors. Effective nerve pain management may also involve targeting the pain modulators, which include endocannabinoids the CB receptors, central opioid receptors, nerve growth factors, and glial cells.[44]

Anticonvulsant and antidepressant drugs are considered the first line treatment of neuropathic pain.

TRYCYCLIC ANTIDEPRESSANT

Trycyclic antidepressant such amitriptyline and imipramine are useful for treating neuropathic pain because they prevent serotonin and noradrenaline from entering the ascending analgesic pathways.[45] The widespread systemic effects involving other receptors, such as the cholinergic and histaminergic, which might result in cardiorespiratory effects, glaucoma, and urine retention, may impair the favorable effects of mentioned drugs, though. Modern medication with less affinity for cholinergic and histaminergic receptors including venlafaxine and duloxetine, increase both serotonin and norepinephrine activity in the pathways that control pain. There are less adverse effect with venlafaxine and duloxetine for treating painful polyneuropathies and diabetic neuropathy.[46]

PHARMACOLOG AND MECHANISM OF ACTION

TCAs exert their effects by modulating around 5 distinct neurotransmitter pathways. These medications function by inhibiting serotonin and norepinephrine reuptake within the presynaptic terminals, resulting in elevated concentrations of these neurotransmitters within the synaptic cleft.

The increased levels of norepinephrine and serotonin in the synapse can contribute to the antidepressant effect. In addition, the neurotransmitters act as competitive antagonists on postsynaptic cholinergic (alpha-1 and alpha-2), muscarinic, and histamine receptors (H1).[47,48] The molecular structure of each receptor significantly impacts TCA's affinity for each of these receptors. The chemical structure of a TCA comprises a 3-ringed arrangement with an attached secondary or tertiary amine. Desipramine, nortriptyline, and protriptyline are categorized as secondary amines, whereas amitriptyline, clomipramine, doxepin, imipramine, and trimipramine belong to the group of tertiary amines. Tertiary amines typically exhibit significant serotonin reuptake inhibition, whereas secondary amines display heightened inhibition of norepinephrine uptake.[49] The inhibition of norepinephrine and serotonin reuptake is believed to underlie the mechanism of TCA utilization in treating neuropathic pain and headache.

ANTI-CONVULSANT

Such as pregabalin and gabapentin are recommended as the first-line treatment for neuropathic pain. It has been discovered that anti-convulsant including carbamazepine, sodium valproate, oxcarbazepine, topiramate, vigabatrin, and levetiracetam have analgesic effects because they increase GABA activity, reduce glutamate release, block NMDA receptors, and block Ca and Na channels on neuronal membranes.[51] Trigeminal neuralgia can be effectively treated with carbamazepine and oxcarbazepine. However, it has not yet been established that the use of more modern anticonvulsants is more effective than using conventional analgesics to treat neuropathic pain or any other type of pain syndrome. Dextromethorphan, amantadine, memantine, and ketamine, as well as substances with variable degrees of NMDA antagonism, have all been shown to be effective analgesics.[52] The need for further research into an NMDA antagonist with high efficacy and fewer side effects arise from the fact that NMDA antagonism causes undesirable psychological side effects, which become more severe with systemic treatment. The aforementioned analogues, are now known to more specifically bind with voltage gated calcium channels and suppress glutamate release at presynaptic and post synaptic locations, both peripherally and centrally.[53] Studies have shown these agents to relieve painful diabetic neuropathy and paroxysmal attacks in trigeminal neuralgia. Subsequent studies have shown the anticonvulsant gabapentin to be effective in painful diabetic neuropathy, mixed neuropathies, and postherpetic neuralgia. Lamotrigine, a new anticonvulsant, is effective in trigeminal neuralgia, painful peripheral neuropathy, and post-stroke pain. Other anticonvulsants, both new and old, are currently undergoing controlled clinical testing. The most common adverse effects of anticonvulsants are sedation and cerebellar symptoms (nystagmus, tremor and incoordination). Less common side-effects include haematological changes and cardiac arrhythmia with phenytoin and carbamazepine. The introduction of a mechanism-based classification of neuropathic pain, together with new anticonvulsants with a more specific pharmacological action, may lead to more rational treatment for the individual patient with neuropathic pain.

PHARMACOLOGY AND MECHANISM OF ACTION

Sodium channels; Blockade of voltage-gated sodium channels is the most common mechanism of action among currently available AEDs. The established agent's phenytoin and carbamazepine are archetypal sodium channel blockers, a mechanism they share with the newer drugs, lamotrigine, felbamate, topiramate, oxcarbazepine, zonisamide, rufinamide, lacosamide, and eslicarbazepine acetate. There is also anecdotal evidence to suggest that sodium valproate and gabapentin have inhibitory effects on neuronal sodium channels. Voltage-gated sodium channels exist in one of three basic conformational states: resting, open, and inactivated. During a single round of depolarisation, channels cycle through these states in turn (resting to open, open to inactivated, inactivated to resting) and are unable to respond to further depolarisations until sufficient numbers have returned from the inactivated state to the resting state. Antiepileptic agents with sodium channel blocking properties have highest affinity for the channel protein in the inactivated state and binding slows the conformational recycling process. As a result, these drugs produce a characteristic voltage and frequency-

dependent reduction in channel conductance, resulting in a limitation of repetitive neuronal firing, with little effect on the generation of single action potentials.[54] GABAA receptors. Activation of the ionotropic GABAA receptor resulting in an enhanced response to synaptically released GABA is a major AED mechanism. Barbiturates (e.g. phenobarbital, primidone) and benzodiazepines (e.g. diazepam, clobazam, clonazepam) share this effect, but they bind to distinct sites on the receptor complex and differentially influence the opening of the chloride ion pore. All GABAA receptors containing at least one alpha- and one beta-subunit appear susceptible to activation by barbiturates, with only minor differences in relative sensitivity. In contrast, benzodiazepines display a much more distinct pattern of selectivity. Benzodiazepine-sensitive GABAA receptors are typically composed of two alpha subunits (alpha1, alpha2, alpha3 or alpha5), two beta-subunits (beta2 or beta3), and a gamma2 subunit, whereas the delta-containing GABAA receptor which mediates tonic inhibition is entirely insensitive to benzodiazepines, as are those containing alpha4- and alpha6-subunits. Functionally, barbiturates increase the duration of chloride channel opening, while benzodiazepines increase the frequency of opening.[54]

Table 2: TREATMENT FOR PERIPHERAL NEUROPATHY.[58]

DRUG NAME	DOSING RANGE	AADVERSE EFFECTS
Gabapentin	3 00-3,600 mg daily in 3 divided doses	Dizziness, somnolence, GI-upset, peripheral edema
Pregabalin	50-300mg daily in 2 or 3 divided doses	Dizziness, somnolence, weight gain
Tricyclic antidepressants (amitriptyline, desipramine, nortriptyline)	10-150mg daily usually dosed at bedtime	Drymouth, Blurred vision, constipation
Duloxetine	60-120 mg daily	Nausea, somnolence, dizziness, D decreased appetite, constipation
Tramadol	50-100mg every 4-6hr	Nausea, vomiting, itchines, dizziness
Lidocaine	Apply patch to affected area; patch may remain in place upto 12hr	Skin irritation
Capsaicine	Apply topically to affected area 3-4 times daily	Stinging and burning sensation

ANASTHESIA DRUGS

For drugs like lidocaine, aberrant buildup of sodium channels is a contributing factor in the abnormal electrical activity in damaged neurons and neuromas. Consequently, a sodium channel-blocking medication may aid in neuropathic pain relief. These drugs include oral mexiletine (which has mechanism of action similar to that of lidocaine), intravenous lidocaine (which also inhibits C-fibers input), and oral tocainide.[56] Baclofen, a GABAB-receptor agonist, has been demonstrated to be useful for treating neuropathic pain as a result of the key role the GABA system in the spinal cord plays in modifying pain management.

CAPSAICINE

It is a topical agent which can be used as backup treatment option. Transient receptor potential cation channel subfamily V member 1, sometimes referred to as vanilloid receptor 1 (TRPV), is a powerful receptor agonist that is produced by capsaicin. Due to their complexity in follow-up and monitoring as well as their possible negative side effects from drug usage, oxycodone and morphine are potent opioids that are advised as third-line treatment.

NON-PHARMACOLOGICAL TREATMENT

Although many patients with neuropathic pain pursue complementary and alternative treatment, rigorous evidence supporting the efficacy of non-drug therapy is limited. Some reports suggest benefits of conservative interventions such as Transcutaneous Electrical Nerve Stimulation, Percutaneous Electrical Nerve Stimulation, acupuncture and others.

ACUPUNCTURE

Inserting tiny needles into various body sites may lessen the symptoms of peripheral neuropathy. It can take several sessions before you start to see progress. When carried out by a licensed professional using sterile needles, acupuncture is typically regarded as safe. There is no clinical trial that shows the efficiency of acupuncture in the treatment of neuropathic pain.[59]

HERBS

Some plants, such evening primrose oil, may assist diabetics with neuropathy experience less pain.

AMINO ACID

Individual with diabetes and those who have had chemotherapy may benefit from amino acids like acetyl-L-carnitine. Chemotherapy can cause nausea and vomiting in patients. Amino acids like acetyl-L-carnitine can help in reducing this nausea and vomiting in patients.

OTHER THERAPIES

TENS stands for Transcutaneous Electrical Nerve Stimulation. Various frequencies of a mild electic current are delivered to the skin through electrodes. For roughly a month, TENS should be used for 30 minutes per day for pain reduction.[60]

PHYSICAL THERAPY

It can help with movement improvement if muscle weakness is apparent, requiring a cane, walker or hand or foot braces.

SURGERY

It is necessary to relieve the strain on nerves if it is the cause of neuropathies, such as pressure from tumors. A nerve block is an injection of medication close to a targeted nerve or a group of nerves to provide temporary pain relief. A permanent nerve block is irreversible, while a temporary nerve block is reversible.

NON-INVASIVE TRANSCRANIAL BRAIN STIMULATION TREATMENT

Patients with refractory neuropathic pain may benefit from non-invasive transcranial brain stimulation treatments such as repetitive Transcranial Magnetic Stimulation (rTMS) and Transcranial Direct Current Stimulation (tDCS). Through a brief magnetic field, rTMS causes electrical currents to flow through the cortex. According to a landmine victim study on Phantom Limb Pain (PLP), high-frequency rTMS (10Hz) can dramatically lessen the discomfort for up to 15 days after treatment. Although the efficacy of rTMS and high-frequency SCS has been demonstrated in patients who have failed to respond to conventional medical care[61], much more research has to be done in this area.

CERVICAL SPINAL CORD STIMULATION (SCS)

Another alternative therapy for those who don't respond to conventional medicine is SCS. SCS, also known as dorsal column stimulation, is an invasive procedure that includes stimulating the spinal cord's dorsal columns with electrical impulses at frequencies of about 50 Hz (administered by an implanted pulse generator) in order to reduce the overexcitability of the brain's neurons.[62] The electrodes can be implanted surgically by a laminotomy or percutaneously using an epidural needle. The use of SCS has led to successful treatments for a number of neuropathic pain syndromes.

2. METHODOLOGY

STUDY DESIGN

A Prospective Observational Study.

DURATION OF STUDY

6 months after the approval of Institutional Ethics Committee.

STUDY SETTING

The study was conducted in the Department of Neurology, Cosmopolitan Hospital, Post Graduate Institute of Health Science and Research, Thiruvananthapuram, Kerala.

STUDY POPULATION

Those patients admitted in Neurology department during the period of 2023-2024 and those who satisfy the inclusion and exclusion criteria.

CRITERIA FOR ELIGIBILITY

INCLUSION CRITERIA

- Age criteria above 18 years.
- Patients with peripheral neuropathy is diagnosed by concerned neurologist according to the criteria as
- Possible peripheral neuropathy
- Probable peripheral neuropathy
- Confirmed peripheral neuropathy
- Patients with a score of greater than 12 in Leeds assessment of neuropathic symptoms and signs scale

EXCLUSION CRITERIA

- Pregnant women.
- Psychiatric patients.
- Patients who are not willing to participate in the study.

SAMPLE SIZE

A total of 77 samples needed for the study.

STUDY PROCEDURE

- This prospective observational study was intended to carryout in peripheral neuropathic patients in neurology department. Study was carried out after getting clearance from institutional ethical committee.
- Patients satisfying the inclusion and exclusion criteria and who were willing to participate in the study were included after obtaining their informed consent.
- Data collection form was used for recording demographic details, clinical presentation and drugs prescribed.
- LANSS was used to assess whether the pain is of neuropathic origin.
- The prescription of each patient was analysed.
- Proper Counselling were provided to patients or caregivers.
- The quality of life of the patients was assessed using Neuro quality of life scale before and after providing patient counselling and the patient was followed up after 1 month.

STASTICAL ANALYSIS

- Statistical analysis was performed using Microsoft Excel.
- Paired t-test was used to analyse the improvement in quality of life before and after providing counselling and education.

DATA COLLECTION TOOL

- Pre designed Data Collection Form
- Informed Consent Form
- Patient Information Sheet
- Leeds assessment of neuropathic symptoms and sign scale
- Neuro-QoL Scale
- Patient Information Leaflet

3. RESULTS AND DISCUSSION

3.1 RESULTS

As per the study criteria 77 patients were enrolled in to the study from neurology department. Prescriptions were analysed. Most commonly prescribed drugs were anticonvulsant like Pregabalin, Gabapentin, Lacosamide along with Methylcobalamin. The study aims to improve the quality of life of patients. During the study period 77 patients were completely followed up.

3.1.1 AGE WISE DISTRIBUTION

Table 3.1.1: Distribution of Age.

Age in years	Number of patients	Mean %
40-50	13	17%
50-60	33	43%
60-70	17	22%
70 -80	14	18%
Total	77	100%

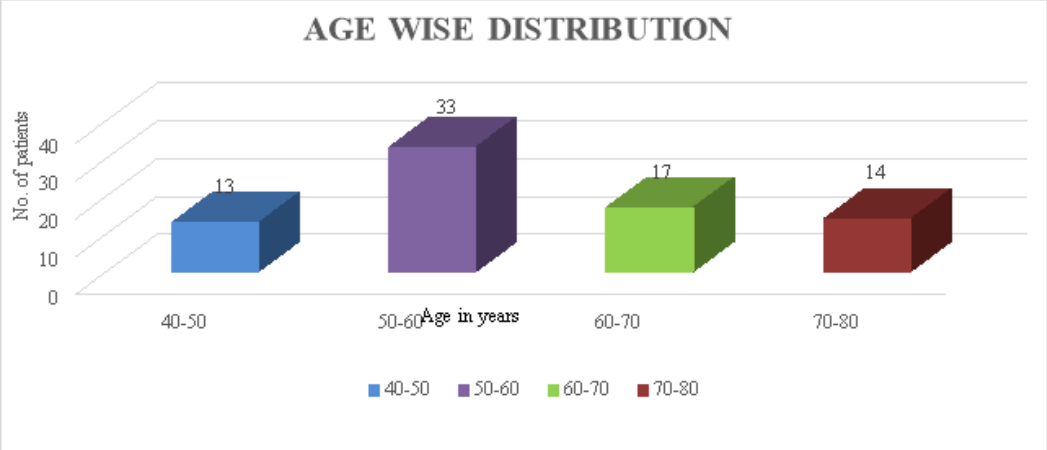

Fig 3.1.1: Age wise distribution.

As per the demographic data of the study population, peripheral neuropathic patients were found to be more in the age group of 50-60 years(43%), 17% belongs to age group of 60-70years and 14% in the age group of 70-80 years.

3.1.2 GENDER WISE DISTRIBUTION

Table 3.1.2: Distribution of Gender.

Gender	Number of patients	Mean%
Male	35	45.45%
Female	42	54.54%
Total	77	100

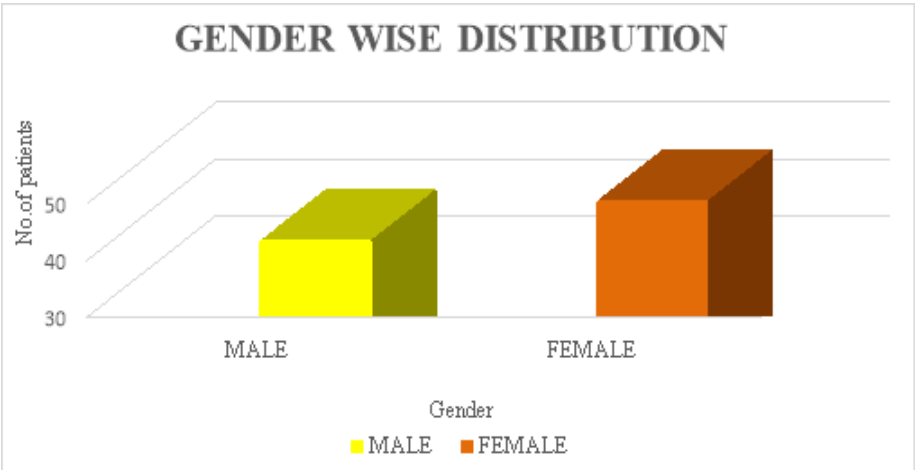

Fig 3.1.2: Gender wise distribution.

Gender wise distribution of the overall study population indicates that female population over- rides male population with 45.45% over 54.54%.

3.1.3 DISTRIBUTION BASED ON SYMPTOMS

Table 3.1.3: Distribution based on Symptoms.

Symptoms	Number of patients	Mean%
Weakness	63	82%
Tingling Sensation	58	75%
Nocturnal Aggravation	20	26%
Numbness	67	87%
Parasthesia	71	92%

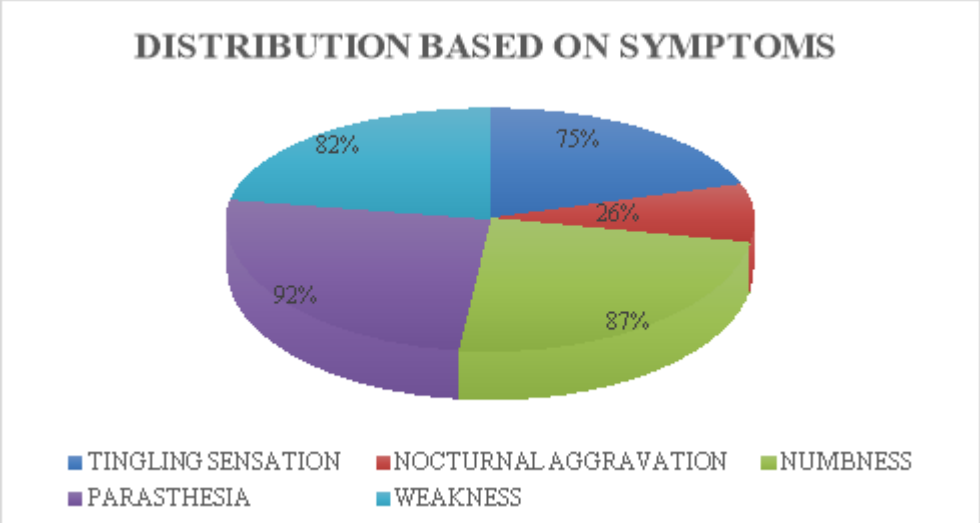

Fig 3.1.3: Distribution based on symptoms.

Out of 77 patients, the majority of them had paraesthesia (92%) followed by numbness (87%) and weakness (82%), 75% had tingling sensation and a small proportion patients have nocturnal aggravation (26%).

3.1.4 DISTRIBUTION BASED ON COMORBIDITIES

Table 3.1.4: Distribution based on comorbidities.

Comorbidities	Number of patients	Mean%
Hypertension	36	47%
Diabetes	76	99%
Heart Disease	28	36%
Thyroid Disease	27	35%
Dyslipidemia	17	22%
Kidney Disease	54	70%

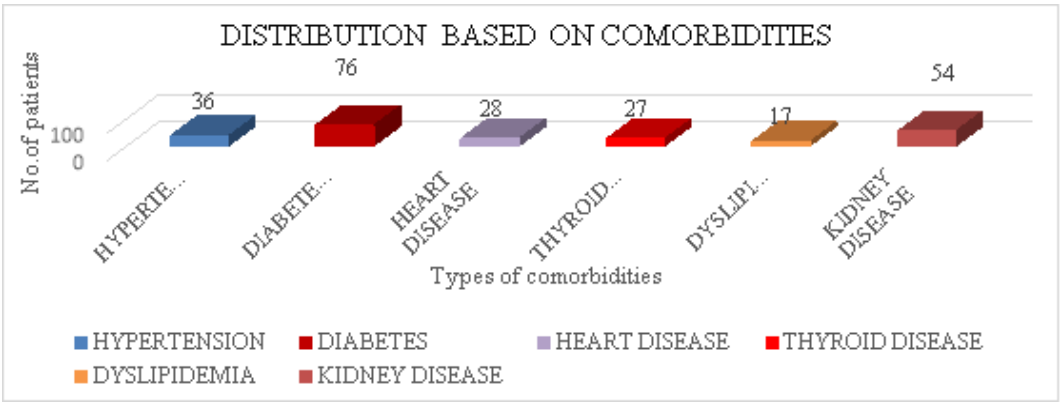

Fig 3.1.4: Distribution based on co morbidities.

Out of 77 patients, the most common co-morbid condition of peripheral neuropathy was found to be Diabetes (99%) followed by kidney disease (70%) and hypertension (47%). A small portion of patients have heart disease (36%), thyroid disease(35%) and dyslipidaemia (22%).

3.1.5 PRESCRIPTION PATTERN

Table 3.1.5: Distribution of drug prescribed.

Drug Prescribed	Number of patients	Mean%
Pregabalin	6	8%
Gabapentin	8	10.3%
Lacosamide	9	11.6%
Pregabalin+Gabapentin	16	21%
Methylcobalamine+Pregabalin	15	19.4%
Methylcobalamine+Gabapentin	11	14.2%
Methylcobalamine+Lacosamide	12	15.5%

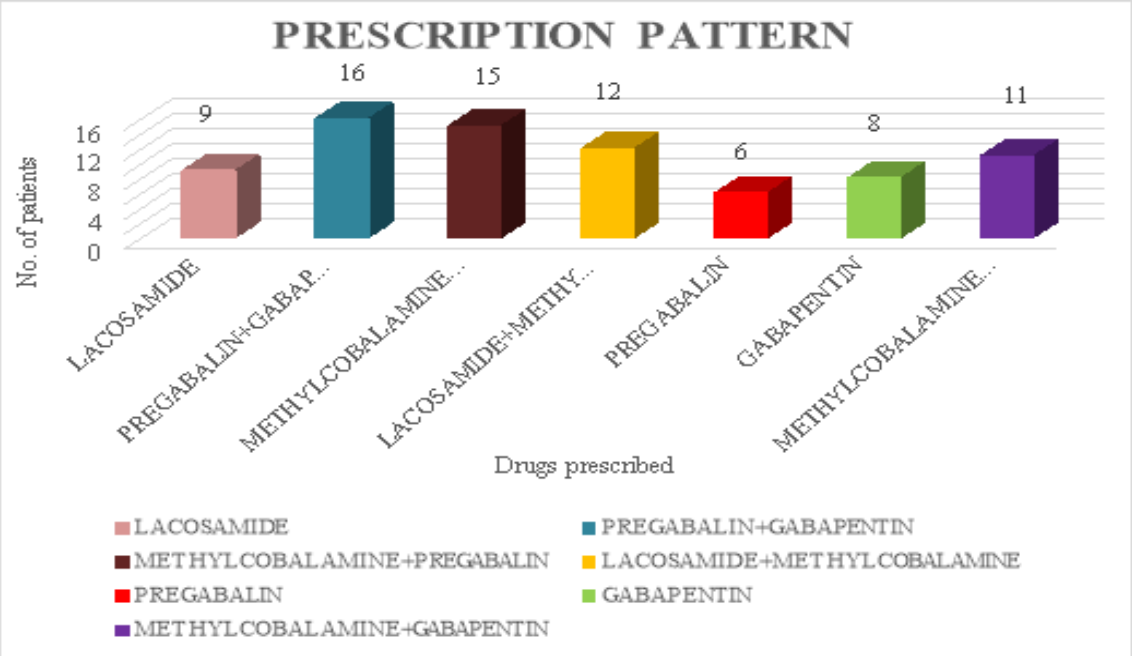

Fig 3.1.5: Distribution of prescribing pattern.

The most commonly prescribed drug for peripheral neuropathy were found to be Pregabalin+Gabapentin(21%),Methylcobalamine+Pregabalin(19.4%)Methylcobalamine+Lacosamide(15.5%),Methylcobalamine+Gabapentin(14.2%),Lacosamide(11.6%), Gabapentin(10.3%) and Pregabalin(8%).

ASSESMENT OF QUALITY OF LIFE BY USING NEURO QOL SCALE

3.1.6 COMPARISON BASED ON COMMUNICATION

Table 3.1.6: Comparison of communication before and after counseling.

Communication	Before	After
Mean Score	20.74	23.51
SD	3.11	2.91
Significant value	0.001* ($p<0.05$)	

When comparing communication, mean score before counselling was found to be 20.74 and after counselling was found to be 23.51. The result was significant and concluded that the communication score after counselling was significantly increased than before counselling.

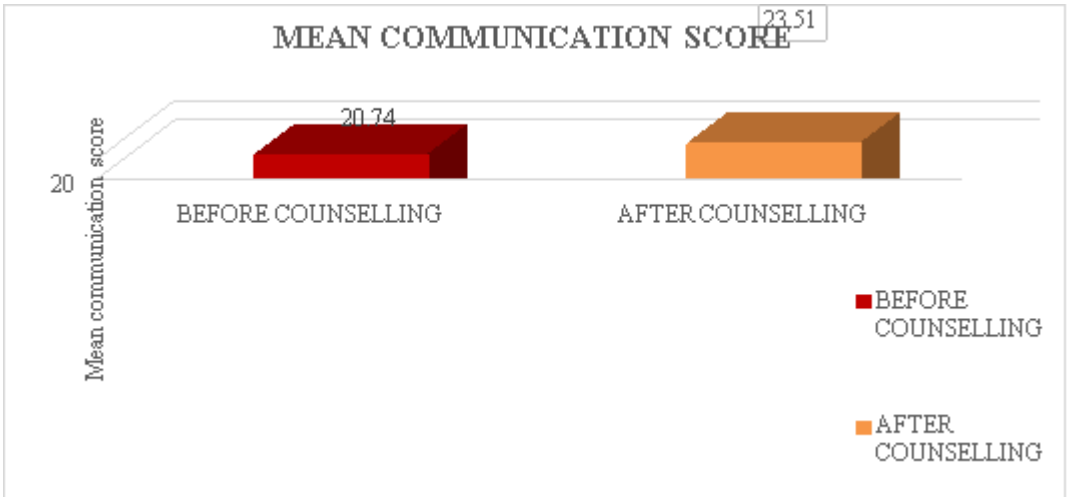

Fig 3.1.6: Comparison of communication before and after counseling.

5.1.7 COMPARISON BASED ON ABILITY TO PARTICIPATE IN SOCIAL ROLES

Table 3.1.7: Comparison of ability to participate in social roles before and after counseling.

Social Roles	Before	After
Mean Score	33.16	35.56
SD	2.70	3.06
Significant value	0.001* (p<0.05)	

When comparing ability to participate in social roles, mean score before counselling was found to be 33.16 and after counselling was found to be 35.56. The result was significant and concluded that the ability to participate in social roles score after counselling was significantly increased than before counselling.

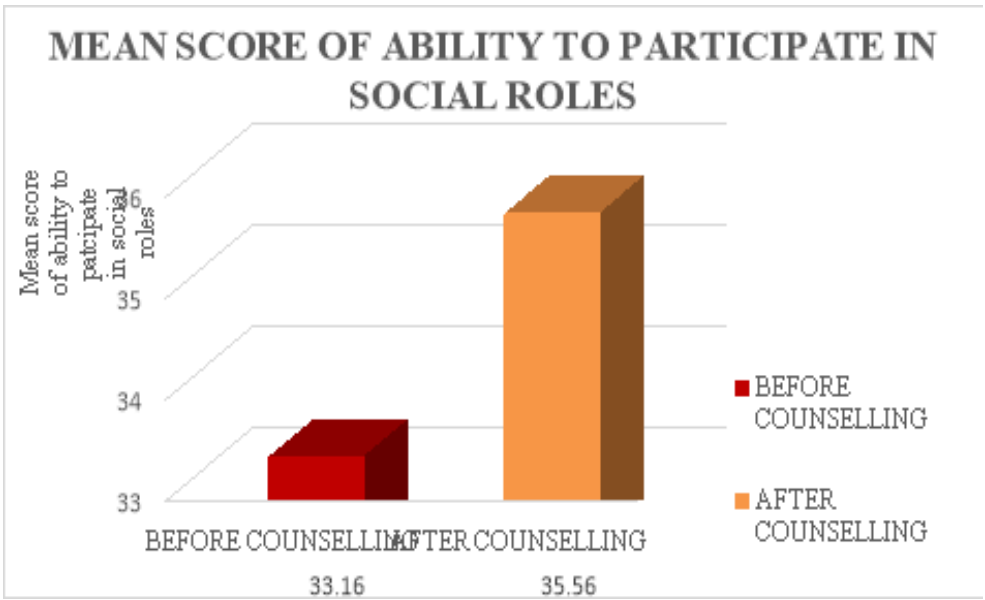

Fig. 3.1.7: Comparison of ability to participate in social roles before and after counseling.

3.1.8 COMPARISON BASED ON ANXIETY

Table 3.1.8: Comparison of anxiety before and after counseling.

Anxiety	Before	After
Mean Score	38.01	35.9
SD	1.90	2.40
Significant value	0.001* (p<0.05)	

When comparing anxiety, mean score before counselling was found to be 38.01 and after counselling was found to be 35.9. The result was significant and concluded that the anxiety score after counselling was decreased than before counselling.

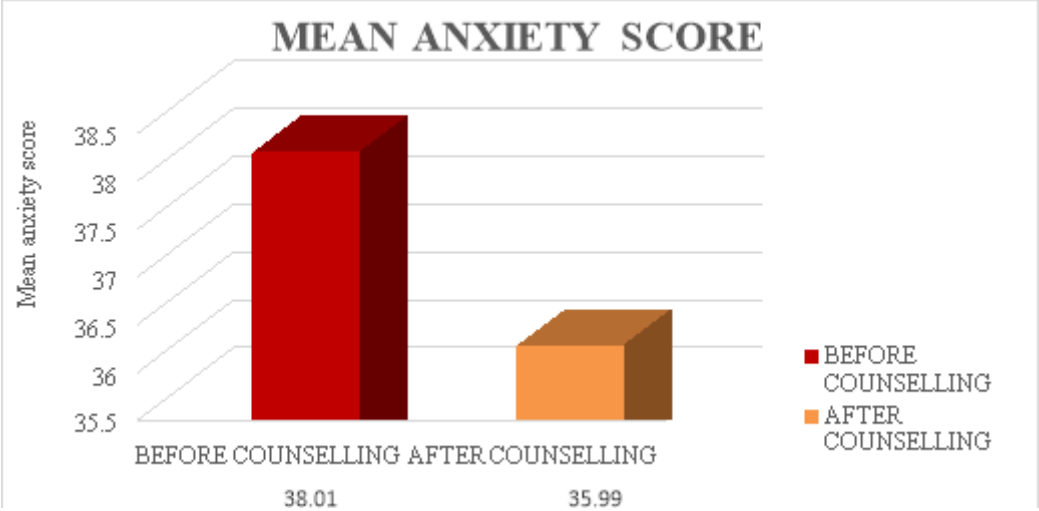

Fig 3.1.8: Comparison of anxiety before and after counseling.

3.1.9 COMPARISON BASED ON DEPRESSION

Table 3.1.19: Comparison of depression before and after counseling.

Depression	Before	After
Mean Score	37.01	35.41
SD	2.02	1.79
Significant value	0.001* (p<0.05)	

When comparing depression, mean score before counselling was found to be 37.01 and after counselling was found to be 35.41. The result was significant and concluded that the depression score after counselling was decreased than before counselling.

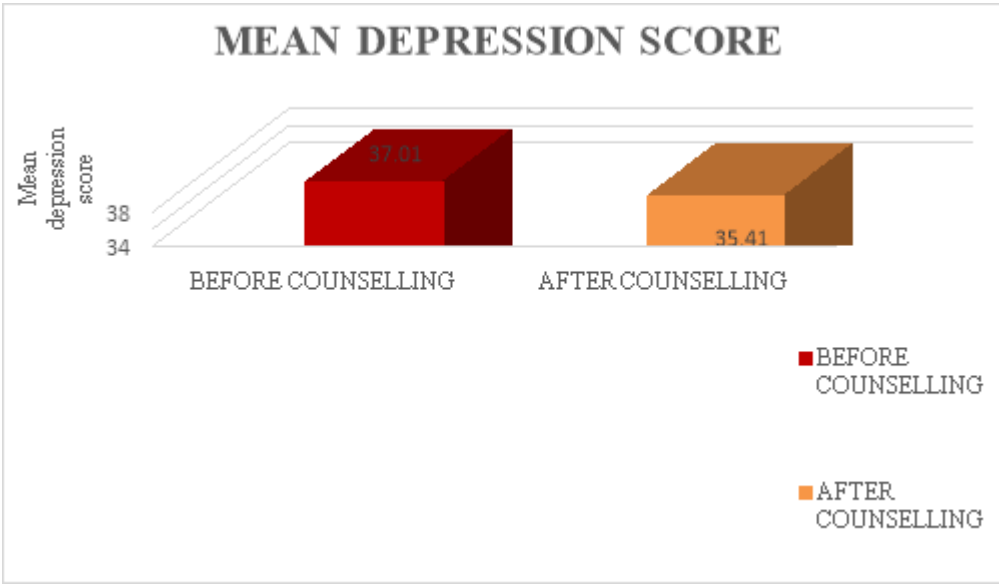

Fig 3.1.9: Comparison of depression before and after counseling.

3.1.10 COMPARISON BASED ON EMOTIONAL AND BEHAVIOURAL DYSFUNCTION

Table 3.1.10: Comparison of emotional and behavioural dysfunction before and after counseling.

Emotional	Before	After
Mean Score	36.77	35.36
SD	2.18	1.91
Significant value	0.001* (p<0.05)	

When comparing emotional and behavioural dysfunction, mean score before counselling was found to be 36.77 and after counselling was found to be 35.36. The result was significant and concluded that the emotional and behavioural dysfunction score after counselling was decreased than before counselling.

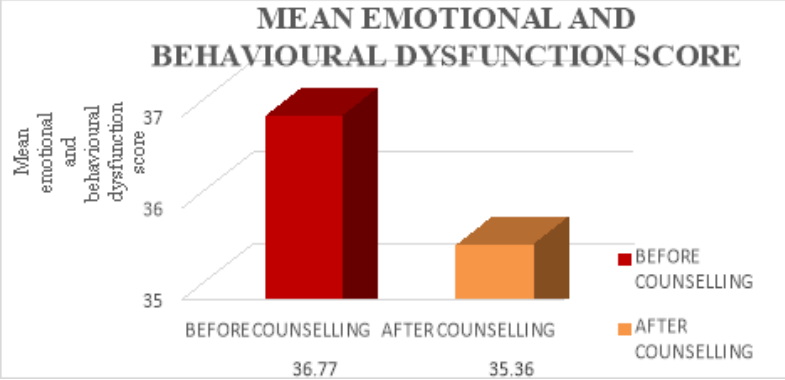

Fig 5.1.10: Comparison of emotional and behavioural dysfunction before and after counseling.

3.1.11 COMPARISON OF FATIGUE

Table 3.1.11: Comparison of fatigue before and after counseling.

Fatigue	Before	After
Mean Score	33.22	31.26
SD	1.20	3.53
Significant value	0.001* (p<0.05)	

When comparing fatigue, mean score before counselling was found to be 33.22 and after counselling was found to be 31.26. The result was significant and concluded that the fatigue score after counselling was decreased than before counselling.

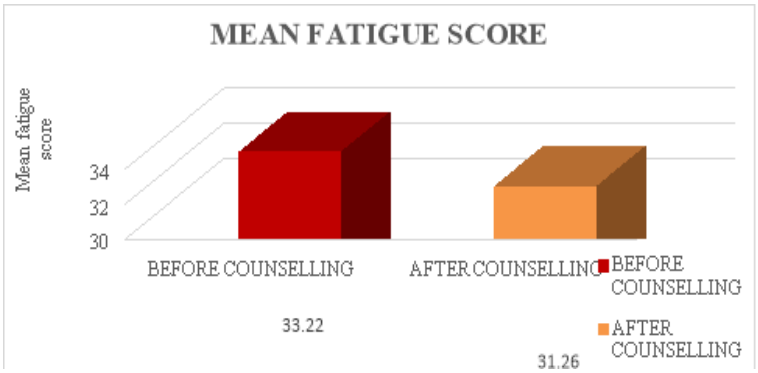

Fig 5.1.11: Comparison of fatigue before and after counseling.

3.1.12 COMPARISON BASED ON LOWER EXTREMITY FUNCTION

Table 5.1.12: Comparison of lower extremity function before and after counseling.

LE function	Before	After
Mean Score	24.80	28.90
SD	4.32	4.43
Significant value	0.001* (p<0.05)	

When comparing lower extremity function, mean score before counselling was found to be 24.80 and after counselling was found to be 28.90. The result was significant and concluded that the lower extremity function score after counselling was significantly increased than before counseling.

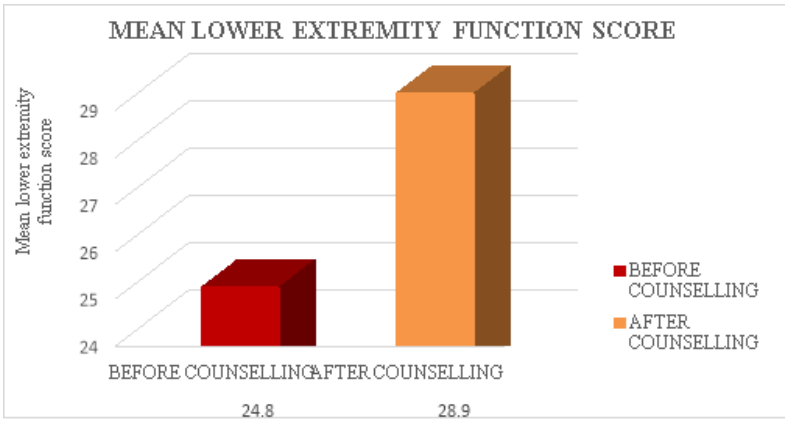

Fig 3.1.12: Comparison of lower extremity function before and after counseling.

3.1.13 COMPARISON BASED ON POSITIVE AFFECT AND WELL-BEING

Table 3.1.13: Comparison of positive affect and well-being before and after counseling.

Well-being	Before	After
Mean Score	28.36	31.05
SD	2.97	3.03
Significant value	0.001* (p<0.05)	

When comparing positive affect and wellbeing, mean score before counselling was found to be 28.36 and after counselling was found to be 31.05. The result was significant and concluded that the positive affect and well being score after counselling was significantly increased than before counseling.

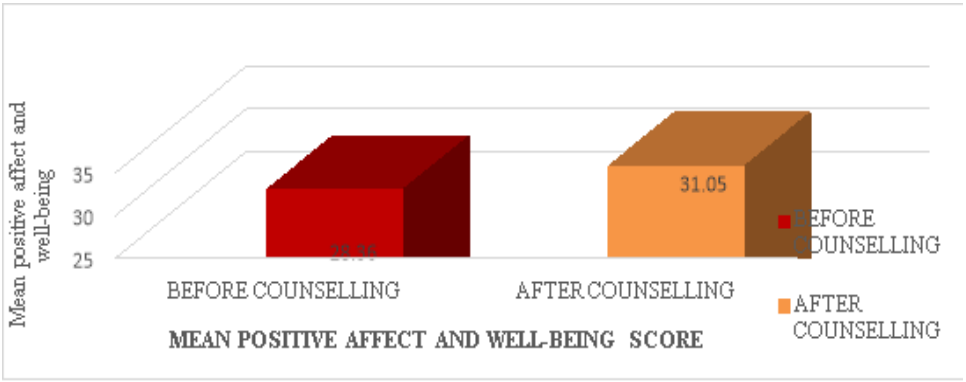

Fig 3.1.13: Comparison of positive affect and well-being before and after counseling.

3.1.14 COMPARISON BASED ON SLEEP DISTURBANCE

Table 3.1.14: Comparison of sleep disturbance before and after counseling.

Sleep disturbance	Before	After
Mean Score	26.77	22.30
SD	7.45	6.75
Significant value	0.001* (p<0.05)	

When comparing sleep disturbance, mean score before counselling was found to be 26.77 and after counselling was found to be 22.30. The result was significant and concluded that the sleep disturbance score after counselling was decreased than before counselling.

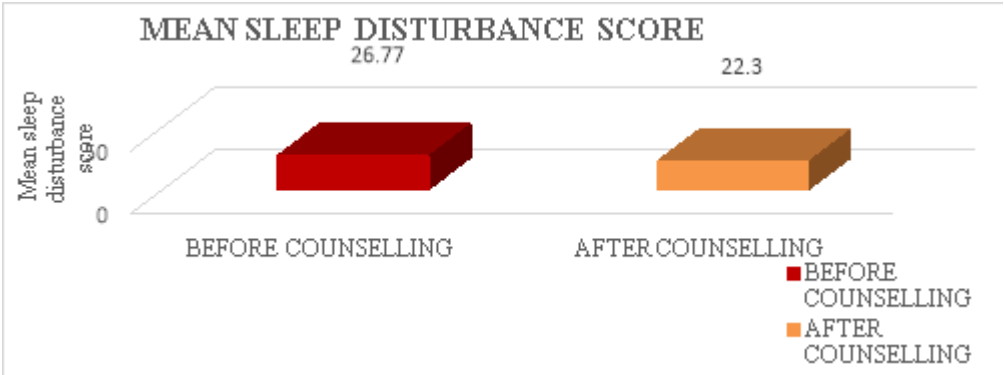

Fig 3.1.14: Comparison of sleep disturbance before and after counseling.

3.1.15 COMPARISON BASED ON UPPER EXTREMITY FUNCTION

Table 3.1.15: Comparison upper extremity function before and after counseling.

Upper extremity function	Before	After
Mean Score	33.83	36.57
SD	2.76	2.22
Significant value	0.001* (p<0.05)	

When comparing upper extremity function, mean score before counselling was found to be 33.83 and after counselling was found to be 36.57. The result was significant and concluded that the upper extremity function score after counselling was significantly increased than before counseling.

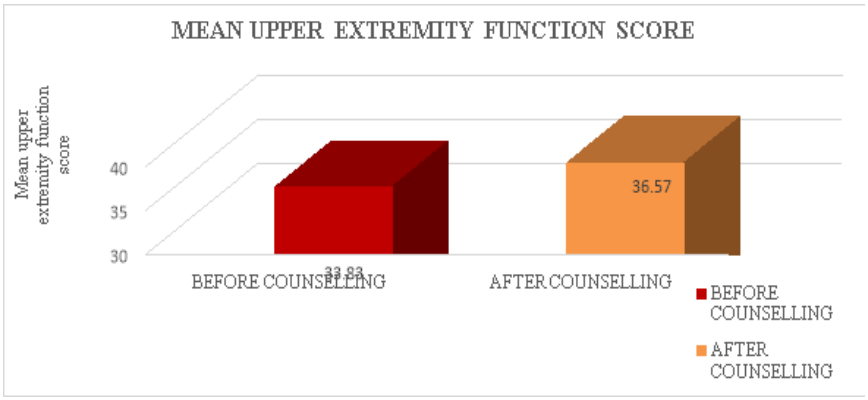

Fig. 3.1.15: Comparison of upper extremity function before and after counseling.

3.1.16 COMPARISON BASED ON STIGMA

Table 3.1.16: Comparison of stigma between before and after counseling.

Stigma	Before	After
Mean Score	9.14	8.39
SD	1.14	0.59
Significant value	0.001* (p<0.05)	

When comparing stigma, mean score before counselling was found to be 9.14 and after counselling was found to be 8.39. The result was significant and concluded that the stigma score after counselling was significantly decreased than before counselling.

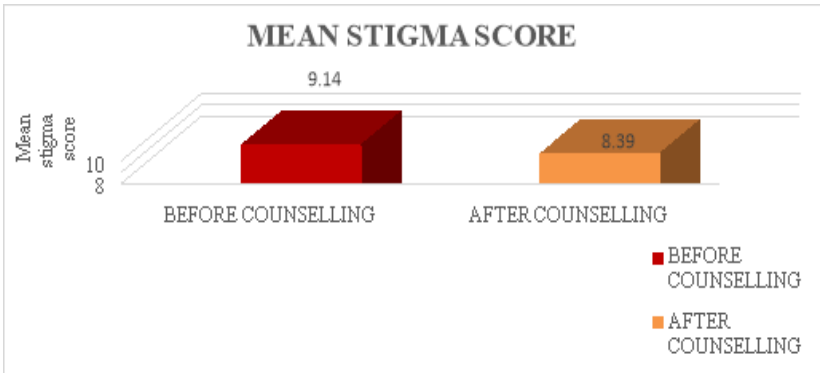

Fig 3.1.16: Comparison of stigma before and after counseling.

3.1.17 COMPARISON BASED ON COGNITION FUNCTION

Table 3.1.17: Comparison of cognition function before and after counseling.

Cognition function	Before	After
Mean Score	34.90	37.27
SD	2.51	2.26
Significant value	.001* (p<0.05)	

When comparing mean cognition function, mean score before counselling was found to be 34.9 and after counselling was found to be 37.27. The result was significant and concluded that the mean cognition function score after counselling was significantly increased than before counseling.

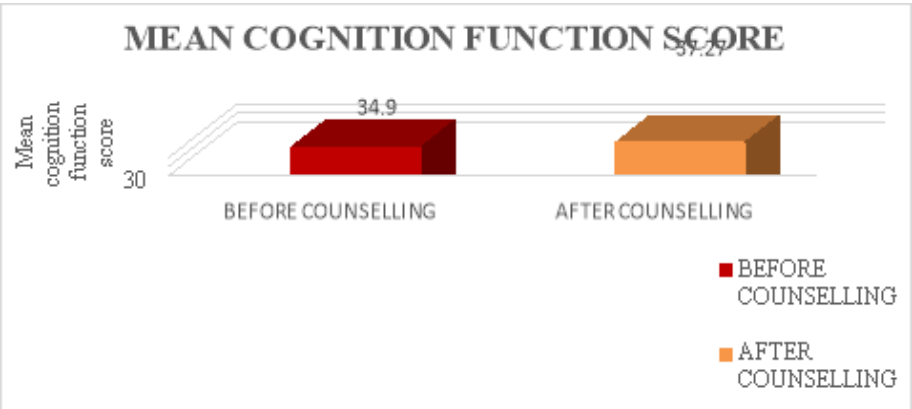

Fig 3.1.17: Comparison of cognition function before and after counseling.

3.2 DISCUSSION

This Prospective observational study was conducted in peripheral neuropathic patients undergoing treatment with the aim of determining the prescribing pattern of drugs and to assess the improvement in the quality of life. Proper counselling was provided to the patient and the impact were assessed. The study was carried out in the Neurology department of Cosmopolitan Hospital Post Graduate Institute of Health Sciences and Research, Thiruvananthapuram. A total of 77 patients were taken for this study. The improvement in the quality of life of the patients was assessed.

3.2.1. AGE

In this study the majority of the patients (43%) comes under the age group of 50-60 years followed by (22%) under the age group of 60-70, then (18%) comes under the age group of 70-80 and (13%) under 40-50 years of age. It is similar to the study conducted by ***"Paul Valensi et al".***[65]

3.2.2. GENDER

In this study the majority of patients (54.54%) were females and (45.45%) were males. It shows that the occurrence of peripheral neuropathy is more in females than in males. It is similar to the study conducted by ***"Melanie L Aaberg et-al"***[66] it shows that the prevalence of peripheral neuropathy tends to be higher in females.

3.2.3. CO-MORBIDITIES

In this study the majority of patients have diabetes mellitus 99%, 77% have kidney disease, 47% have hypertension, 36% have heart disease, 35% have thyroid disease and 22% have dyslipidaemia. It shows that diabetes is the leading cause for development of peripheral neuropathic pain. It is similar to the study conducted by "***Aleppo et al".***[67]

3.2.4. SYMPTOMS

In this study iIt was observed that out of 77 patients 92% of them experience paraesthesia, 87% have complaints of numbness, 75% had tingling sensation and 26% had nocturnal aggravation. It is similar to the study conducted by ***"R Beran et-al"***[68] which concluded that paraesthesia is often accepted as the hallmark symptom for neuropathy.

3.2.5. PRESCRIPTION PATTERN

The most commonly prescribed drug for peripheral neuropathy were found to be Pregabalin+Gabapentin(21%), Methylcobalamine+Pregabalin(19.4%)Methylcobalamine+Lacosamide(15.5%), Methylcobalamine+Gabapentin(14.2%),Lacosamide(11.6%), Gabapentin(10.3%) and Pregabalin(8%). **"*Parvan Banu et-al".***[69]

3.2.6. QUALITY OF LIFE

In this study, Neuro QOL scale with 12 domains were used to assess the quality of life of the patients. It shows that after providing proper counselling about the disease, drugs and life style modifications there was a significant improvement in the quality of life of patients.

4. CONCLUSION

Peripheral neuropathy happens when the nerves that are located outside of the brain and spinal cord (peripheral nerves) are damaged. This condition often causes weakness, numbness and pain usually in the hands and feet. People with peripheral neuropathy usually describe the pain as stabbing, burning or tingling sensation. Medicines can reduce the pain of peripheral neuropathy. Peripheral neuropathy can affect one nerve, called mononeuropathy. If it affects two or more nerves in different areas, it is called multiple mononeuropathy, and if it affects many nerves, it is called polyneuropathy.

A single centered prospective observational study was conducted in Neurology Department of Cosmopolitan Hospital, Post Graduate Institute and Health Sciences, Thiruvananthapuram. Based on the inclusion and exclusion criteria 77 patients with peripheral neuropathic pain were enrolled in this study. A significant proportion of the study participants were aged between 50-60 years. The analysis also covered gender distribution, symptomatic distribution, and comorbidities. It is also noted that females are more commonly affected than males, and paraesthesia is the most prevalent symptom associated with peripheral neuropathy.

The study demonstrates the prescribing pattern of drugs in peripheral neuropathic patients, based on the study the most commonly prescribed drugs were found to be Methyl cobalamin followed by Lacosamide, Pregabalin and Gabapentin. This study also signifies the improvement in the quality of life of the patients with neuropathic pain after providing proper counselling to the patients.

REFERENCE

1. Study protocol for the World Health Organization project to develop a Quality of Life assessment instrument (WHOQOL). Qual Life Res., Apr. 1993; 2(2): 153-9.
2. Cella D, Lai JS, Nowinski CJ, Victorson D, Peterman A, Miller D, Bethoux F, Heinemann A, Rubin S, Cavazos JE, Reder AT, Sufit R, Simuni T, Holmes GL, Siderowf A, Wojna V, Bode R, McKinney N, Podrabsky T, Wortman K, Choi S, Gershon R, Rothrock N, Moy C. Neuro-QOL: brief measures of health-related quality of life for clinical research in neurology. Neurology, Jun. 5, 2012; 78.
3. Bennett M. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. Pain, May 2001; 92(1-2): 147-57.
4. Sullivan MD, Tutelman PR, Ushida T, Vader K. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain, Sep. 1, 2020; 161(9).

5. Szok D, Tajti J, Nyári A, Vécsei L. Therapeutic Approaches for Peripheral and Central Neuropathic Pain. Behav Neurol, Nov 21, 2019; 2019: 8685954.
6. Marchettini P, Lacerenza M, Mauri E, Marangoni C. Painful peripheral neuropathies. Curr Neuropharmacol, Jul. 2006; 4(3): 175-81.
7. Amanda C, Williams C, Kenneth D. Updating the definition of pain. Class if Chronic Pain. 209-14.Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain., 2020; 161(9): 1976-82.
8. Gibson S, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain., 2020; 161(9): 1976-82.
9. Caterina MJ, Julius D. The vanilloid receptor: A molecular gateway to the pain pathway.Annu Rev Neurosci, 2001; 24(1): 487-517.
10. Bag AK, Hiremath SR. Neuropathic Pain and its Management. Indian Journal of Pharmacy Practice, 2023; 16(3).
11. Kaur J, Ghosh S, Sahani AK, Sinha JK. "Mental Imagery as a Rehabilitative Therapy for Neuropathic Pain in People With Spinal Cord Injury: A Randomized Controlled Trial". Neurorehabilitation and Neural Repair, November 2020; 34(11): 1038–1049.
12. Diabetic neuropathy-causes and treatments SPA soundpainalliance image.
13. "Volume 12, Spring 1999 | University of Pennsylvania Orthopaedic Journal". Retrieved 2019-10-28.
14. Dorlands Medical Dictionary:mononeuropathy".
15. Amato AA, Ropper AH. "Sensory Ganglionopathy". New England Journal of Medicine, 22 October 2020; 383(17): 1657–1662.
16. Gwathmey KG. "Sensory neuronopathies". Muscle & Nerve, January 2016; 53(1).
17. Sugimoto K, Yasujima M, Yagihashi S. "Role of advanced glycation end products in diabetic neuropathy". Current Pharmaceutical Design, 2008; 14(10): 953–61.
18. Ball DA. "Peripheral Neuropathy". NeuraVite. Retrieved 24 March 2016.
19. Vinik AI, Erbas T. "Diabetic autonomic neuropathy". Autonomic Nervous System. Handbook of Clinical Neurology, 2013; 117: 279–94.
20. Gambeta E, Chichorro JG, Zamponi GW. Trigeminal neuralgia: An overview from pathophysiology to pharmacological treatments. Mol Pain., Jan-Dec, 2020; 16.
21. Trigeminal neuralgia (TN) ;https://www.linkedin.com/pulse/trigeminal-neuralgia-tn-suicidal-disease-physio-plus-jtiuc.
22. Aggarwal A, Suresh V, Gupta B, Sonthalia S. Post-herpetic Neuralgia: A Systematic Review of Current Interventional Pain Management Strategies. J Cutan Aesthet Surg, Oct-Dec. 2020; 13.
23. https://images.app.goo.gl/cXKcnha7XWrdFntg9 Anatomy of shingles-the shingles viruses.
24. J Bodyw Mov, Complex regional pain syndrome—1: history, diagnostic criteria and etiology, 2004; 167-177.
25. Darivemula, Surendra; Nagoor, Khadervali; Patan, Shakeer Khan; Reddy, N. Bayapa; Deepthi, C. Sravana; Chittooru, Chandra Sekhar. Prevalence and Its Associated Determinants of Diabetic Peripheral Neuropathy (DPN) in Individuals Having Type-2 Diabetes Mellitus in Rural South India. Indian Journal of Community Medicine, Apr–Jun. 2019; 44(2): 88-91.
26. Viswanath O, Urits I, Burns J, Charipova K, Gress K, McNally A, Urman RD, Welschmeyer A, Berger AA, Kassem H, Sanchez MG, Kaye AD, Eubanks TN, Cornett EM, Ngo AL. Central Neuropathic Mechanisms in Pain Signaling Pathways: Current Evidence and Recommendations. Adv Ther., May 2020; 37(5): 1946-1959.
27. Dipika bansal;, Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabets mellitus in a tertiary care settings, Feb 2014.
28. Woolf CJ, Mannion RJ. Neuropathic pain: aetiology, symptoms, mechanisms, and management. The lancet, Jun. 5, 1999; 353(9168): 1959-64.
29. Bennett MI, Rayment C, Hjermstad M, Aass N, Caraceni A, Kaasa S. Prevalence and aetiology of neuropathic pain in cancer patients: a systematic review. Pain, Feb. 1, 2012; 153(2): 359-65.
30. Syahfitri Hanum A, Nandar Kurniawan S. DRUG INDUCED NEUROPATHY. JPHV [Internet]. 2023 Oct. 9 [cited 2024 May 19];
31. Roger bannister:Brain and Bannisters Clinical Neurology :7th edirion., 430-457.
32. Liu X, Xu Y, An M, Zeng Q. The risk factors for diabetic peripheral neuropathy: A meta-analysis. PLoS One, Feb. 20, 2019; 14.
33. Bodman MA, Dreyer MA, Varacallo M. Diabetic Peripheral Neuropathy. [Updated 2024 Feb 25.
34. Dr brian c callaghan; Diabetic neuropathy:clinical manifestation and current treatments, june 2012.
35. https://www.amarapain.com/numbness-in-the-leg/ neuropathic signs and symptoms
36. i D, Jiaqi L, Jinxuan R, Bin Z, Chengwei W, Lina Y. NAD+ metabolism in peripheral neuropathic pain. Neurochem Int., 2022; 161: 1-13.
37. Sachau J, Sendel M, Péchard M, Schnabel K, Schmieg I, Medkour T, et al. Patient reported outcome measures in chronic neuropathic pain clinical trials-A systematic literature review. J Pain., 2023; 24(1): 38-54.
38. Wei J, Chang S, Liu S, Tian L, Zhu X, Wang S, et al. Lysine-specific demethylase in primary sensory neurons participates in chronic compression of dorsal root ganglion–induced neuropathic pain. Brain Res Bull., 2022; 191: 30-9.
39. Jingmei X, Ping L, Feng L, Yulu C, Qulian G, Yong Y. Domino reaction of neurovascular unit in

neuropathic pain after spinal cord injury. Exp Neurol, 2023; 359: 1-6.
40. Kaur S, Bali A, Singh N, Jaggi AS. Demystifying the dual role of the angiotensin system in neuropathic pain. Neuropeptides, 2022; 94: 102260.
41. Cavalli E, Mammana S, Nicoletti F, Bramanti P, Mazzon E. The neuropathic pain: an overview of the current treatment and future therapeutic approaches. Int J Immunopathol Pharmacol, 2019; 33.
42. Kumar Abbas Fausto; Diseases of organ systems; Robbins ana Cotran; Pathologic basis of disease; 7th edition, 1334.
43. Dworkin RH, Malone DC, Panarites CJ, Armstrong EP, Pham SV. Impact of postherpetic neuralgia and painful diabetic peripheral neuropathy on health care costs. J Pain., 2010; 11(4): 360-8. doi: 10.1016/j.jpain.2009.08.005
44. Bouhassira D, Letanoux M, Hartemann A. Chronic pain with neuropathic characteristics in diabetic patients: A French cross-sectional study. PLOS ONE, 2013; 8(9).
45. Cruccu G, Garcia-Larrea L, Hansson P, Keindl M, Lefaucheur JP, Paulus W, et al. EAN guidelines on central neurostimulation therapy in chronic pain conditions. Eur J Neurol, 2016; 23.
46. Robert HD, Alec B. O'C, Joel K, Sean C. Mackey, Srinivasa NR, Brett R. Stacey, et al. Interventional management of neuropathic pain: NeuPSIG recommendations. PAIN, 2013; 154(11).
47. Hillhouse TM, Porter JH. A brief history of the development of antidepressant drugs: from monoamines to glutamate. Exp Clin Psychopharmacol, Feb. 2015; 23(1).
48. Richelson E. Antimuscarinic and other receptor-blocking properties of antidepressants. Mayo Clin Proc., Jan. 1983; 58(1).
49. Gillman PK. Tricyclic antidepressant pharmacology and therapeutic drug interactions updated. Br J Pharmacol, Jul, 2007; 151(6): 737-48.
50. https://images.app.goo.gl/KxFf6yUxPmCykmWQ7 Mechanism of action of tricyclic antidepressants
51. Markman J, Resnick M, Greenberg S, Katz N, Yang R, Scavone J, et al. Efficacy of pregabalin in post-traumatic peripheral neuropathic pain: a randomized, double-blind, placebo-controlled phase 3 trial. J Neurol, 2018; 265(12).
52. Robertson K, Marshman LAG, Plummer D, Downs E. Effect of gabapentin vs pregabalin on pain intensity in adults with chronic sciatica: A randomized clinical trial. JAMA Neurol, 2019; 76(1).
53. Swerdlow M, Cundill JG. Anticonvulsant drugs used in the treatment of lancinating pain. A comparison. Anaesthesia, 1981; 36(12): 1129-32.
54. Graeme J sills; mechanism of action of antiepileptic drugs; Department of molecular and clinical pharamacology chapter 25.
55. https://images.app.goo.gl/C94MG7uyyqbJGNrN6 mechanism of action of anti-convulsant
56. Wi PJ, Knaggs R, Derry S, Cole P, Phillips T, Moore RA. Paracetamol (acetaminophen) with or without codeine or dihydrocodeine for neuropathic pain in adults [review]. Cochrane Database Syst Rev., 2016; 12.
57. Rebecca D, Brett S. Multimodal treatment of chronic pain. Med Clin N Am., 2016; 100(1): 55-64.
58. Elizabeth G.Montfort:Neuropathic pain:A review of diabetic neuropathy, May 20 2010.
59. Patient and caregiver education. managing peripheral neuropathy, 1-9.
60. Neuropathic pain associated with peripheral neuropathy. The voice of the patient. US Food and drug administration.
61. Doth AH, Hansson PT, Jensen MP, Taylor RS. The burden of neuropathic pain: A systematic review and meta-analysis of health utilities. Pain., 2010; 149(2): 338-44.
62. Lanteri-Minet M, Laurent B, Fermanian J, Bouhassira D. The specific disease burden of neuropathic pain: results of a French nationwide survey. Pain, 2011; 152(12): 2836-43.
63. Ian Gilron; Neuropathic pain; a practical guide for the clinician, August 1 2006.
64. Benassayag Kaduri N, Dressler R, Abu Ahmad W, Rotshild V. Trends in Pregabalin Use and Prescribing Patterns in the Adult Population: A 10-Year Pharmacoepidemiologic Study. CNS drugs, Feb. 2024; 38(2): 153-62.
65. Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. The Journal of Pain, Mar. 1, 2005; 6(3): 149-58.
66. Ziegler D, Hidvégi T, Gurieva I, Bongardt S, Freynhagen R, Sen D, Sommerville K, Lacosamide SP743 Study Group. Efficacy and safety of lacosamide in painful diabetic neuropathy. Diabetes Care, Apr. 1, 2010; 33(4): 839-41.
67. Vileikyte L, Peyrot M, Bundy C, Rubin RR, Leventhal H, Mora P, Shaw JE, Baker P, Boulton AJ. The development and validation of a neuropathy-and foot ulcer-specific quality of life instrument. Diabetes care, Sep. 1, 2003; 26(9): 2549-55.
68. Valensi P, Giroux C, Seeboth-Ghalayini B, Attali JR. Diabetic peripheral neuropathy: effects of age, duration of diabetes, glycemic control, and vascular factors. Journal of Diabetes and its Complications, Jan. 1, 1997; 11(1): 27-34.
69. Aaberg ML, Burch DM, Hud ZR, Zacharias MP. Gender differences in the onset of diabetic neuropathy. Journal of Diabetes and its Complications, Mar. 1, 2008; 22(2): 83-7.