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CLINICAL AND ETIOLOGICAL STUDY OF PERIPHERAL NEUROPATHY WITH SPECIAL REFERENCE TO NERVE CONDUCTION STUDY

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ABSTRACT

Background: Peripheral neuropathy refers to any disorder of the peripheral nervous system. It is a common neurological disorder with variable presentations and numerous etiologies. Nerve conduction studies are an extension of clinical history and examination. NCS are less invasive, and are sensitive to both myelin sheath and axonal changes. It is an excellent measure of the function of the PNS and provides a reliable index of measurement in the diagnosis, treatment, and prognosis of the patient.

Objectives: To study the clinical parameters and etiologies in suspected cases of peripheral neuropathy, and its association with nerve conduction study.

Methods: 100 patients of both genders above the age of 18 years, with clinical features suggestive of peripheral neuropathy, were observed to study the etiology and correlate clinical parameters with nerve conduction study to assess the severity of peripheral neuropathy.

Results: Out of 100 subjects, 57 were male and 43 were females (M:F = 1.3:1). Most common clinical presentation in our study was burning/ tingling/ pricking sensation in the limbs, followed by numbness/ loss of sensation. Most common etiology was observed to be diabetes mellitus, followed by chronic ethanol abuse. Majority of patients presenting with burning/ tingling/ pricking sensation revealed mixed sensory motor lesions on the NCS with demyelinating nerve injury.

Conclusion: NCS is a reliable investigation in diagnosis, treatment, and prognosis of peripheral neuropathy. Most frequent presenting symptom was burning/ tingling sensation, followed by numbness. Most common etiology was diabetes, followed by chronic ethanol abuse. We inferred that patients with multiple etiologies of peripheral neuropathy had more severe findings on NCS as compared to those presenting with single etiologies. Majority of patients with mild symptoms were found to have pure sensory demyelinating lesions on NCS, whereas severe neuropathic symptoms revealed mixed sensory motor lesions with axonal and demyelinating injury on NCS. Hence, clinical examination and NCS will guide the clinician to assess the severity of peripheral neuropathy, its prognosis, and promote better management of patients.

Keywords: clinical neurology, etiology, peripheral neuropathy, nerve conduction study, axonal, demyelinating

INTRODUCTION

The peripheral nervous system is the main intermediary between the brain and peripheral tissues. The peripheral nervous system is more exposed to environmental toxins than the central nervous system, and can easily undergo trauma. Peripheral neuropathy refers to any disorder of the peripheral nervous system. Dysfunction in the peripheral nervous system can result from ageing, injury, or disease, including infection and diabetes. Peripheral neuropathy affects 2% - 3% of the population and increases to 8% in the elderly population.

It is a common neurological disorder with variable presentation and numerous etiologies. There are over 100 causes of neuropathy.[1] In India and other developing countries, the incidence of diabetes has increased; therefore, diabetic neuropathy is also on a rising trend. The clinician must determine the underlying treatable cause, which is achieved by adopting a systematic approach.[2] In 50% of the cases, the etiology of neuropathy remained undiagnosed.[3]In addition to clinical examination, nerve conduction study (NCS) is extremely helpful in determining the severity of nerve injury. Using the NCS, peripheral neuropathy is divided into those that primarily affect the myelin sheath and those that primarily affect the axon.[4] The peripheral neurophysiological examination includes nerve conduction studies in addition to clinical history and examination. Indications for nerve conduction studies include evaluating the nature of the pathophysiology, quantifying the severity of involvement, detecting the level of a neurologic deficit, and determining prognosis. Therefore, NCS is a good measurement of overall peripheral nerve health.

Nerve conduction studies are less invasive than many other measurements of health span and can be easily incorporated into longitudinal studies.NCS being sensitive to axonal and a myelin sheath change makes it an excellent measure of the peripheral nervous system function. Nerve conduction studies provide the most sensitive and accurate account of peripheral neuropathophysiology.

METHODOLOGY

Our study was a hospital-based cross-sectional observational study. After approval from the institutional ethics committee, written informed consent was obtained from 100 patients of both genders, above the age of 18 years, presenting to OPD/admitted under medicine department in Rajarajeswari Medical college and Hospital, Bengaluru, with symptoms suggestive of peripheral neuropathy. Critically ill patients and pregnant women were excluded from the study. Each patient was subjected to detailed medical history of symptoms like paraesthesia, tingling sensation, burning feet, hyperaesthesia, loss of sensation, numbness, foot ulcer, weakness, and gait abnormalities. General physical examination and vitals were recorded. All system examination were performed. Motor examination was performed to look for signs such as diminished power and ankle jerk. Sensory examination using monofilament 10g for loss of light touch, superficial pain, and vibration and joint position sensation were examined. Romberg's sign was also elicited. Nerve conduction study of lower limbs were performed in a warm room with the participants in supine position. Nerve conduction velocity data were recorded using a Nihon Kohden Neuropack MEB-9400. Diabetic status was also evaluated, and patients were categorised into 3 groups- those with HbA_1c of <6.5, 6.5 - 8, and >8. Other investigations included complete blood count (CBC), renal function test (RFT), liver function test (LFT), and thyroid function test (TFT). Special investigations, including vitamin D/ vitamin B_{12}/ ANA

profile/ RA factor, were done as and when required. Data was analysed using descriptive and inferential statistics using software MS Excel and SPSS V23.

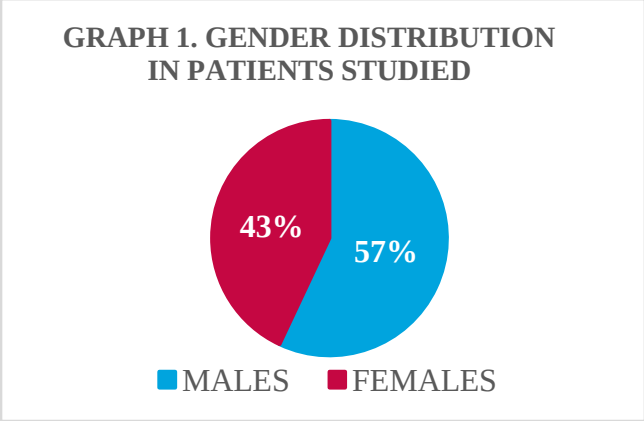
RESULTS

100 subjects of both genders who met the inclusion and exclusion criteria were studied.57 were male, and 43 were females (Graph 1).Out of 100, 67 subjects were in the age group of 35 - 65 years (36 males, 31 females). Mean age was 51.6±13.71. (Graph 2, Table 1)

Most common clinical presentation of peripheral neuropathy in our study was burning/ tingling/ pricking sensation in the limbs (59%). 21% patients presented with loss of sensation/ numbness of limbs and 20% had both. Romberg's was positive in 46 patients.(Graph 3)

Most common etiology was diabetes mellitus (38), followed by chronic alcoholism(15) and vitamin B_{12} deficiency(11). Other causes included hypothyroidism, CIDP, AIDP. One case was diagnosed to have autoimmune myositis. 4 patients had neuropathy of unknown etiology. Diabetes mellitus with superadded hypothyroidism/ vitamin B_{12} deficiency/ vitamin D deficiency/ chronic alcoholism further worsened the presentation of neuropathy features. A total of 55 subjects were diabetics with or without other associated etiologies, out of which 38were of pure diabetic etiology. Similarly, we observed 22 patients with history of chronic alcoholism, with or without associated vitamin B_{12} deficiency. Significant P value was obtained on comparison of peripheral neuropathy cases with HbA_1c > 8%, suggesting that high glycemic status is highly prone to neuropathy. (Table 2,3)

Out of 100 patients studied, 91 NCS were abnormal, and 9 were normal. Abnormal NCS included sensory, motor, axonal and demyelinating lesions in various combinations. Out of 91 abnormal NCS, 20 had pure axonal injury, 44 had demyelinating injury and 27 had mixed axonal demyelinating injury. Out of 59 patients with burning/ tingling sensation, 43 had mixed sensory motor lesions on the NCS, 34 patients had demyelinating nerve injury, 10 had axonal injury, 9 had both axonal and demyelinating injury, whereas 6 were normal. Out of 21 subjects with loss of sensation/ numbness, 13 had mixed sensory and motor involvement, 9 had demyelinating injury, 6 had axonal, 3 had mixed axonal and demyelinating injury, and 3 were normal NCS. Out of 20 patients with both burning/tingling sensation and loss of sensation/ numbness, 17 had mixed sensory motor involvement, and 15 had both axonal and demyelinating lesions. (Table 4)



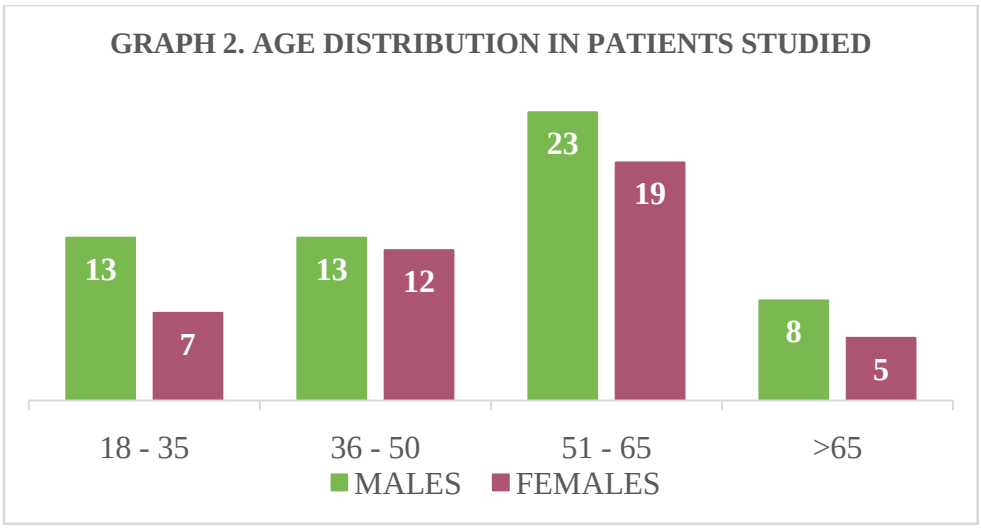


TABLE 1. AGE DISTRIBUTION OF PATIENTS STUDIED

AGE (YEARS)	NUMBER OF PATIENTS			PERCENTAGE
	MALES	FEMALES	TOTAL	
18 - 35	13	7	20	20%
35 – 50	13	12	25	25%
51 – 65	23	19	42	42%
>65	8	5	13	13%

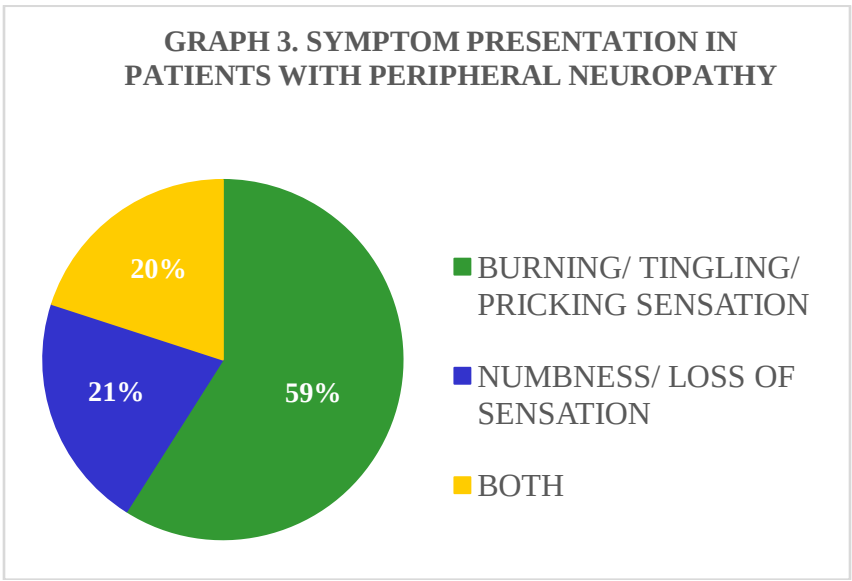


TABLE 2. ETIOLOGY OF PERIPHERAL NEUROPATHY IN PATIENTS STUDIED

SINGLE ETIOLOGY	NUMBER OF PATIENTS	PERCENTAGE
DIABETES MELLITUS	38	38%
ALCOHOL	15	15%
VITAMIN B_{12} DEFICIENCY	11	11%
HYPOTHYROIDISM	4	4%
CIDP	4	4%
AIDP	3	3%
AUTOIMMUNE MYOSITIS	1	1%
UNKNOWN	4	4%
MULTIPLE ETIOLOGY		
DM WITH MULTIPLE ETIOLOGY	55	55%
ALCOHOL WITH B_{12} DEF	22	22%

TABLE 3. HBA_1C LEVELS IN PATIENTS WITH PERIPHERAL NEUROPATHY

HBA_1C	NUMBER OF PATIENTS	PERCENTAGE	P VALUE
<6.5	45	45%	<0.0001
6.5% - 8%	6	6%	0.0306
>8%	49	49%	<0.0001

TABLE 4. NCS PARAMETERS IN PATIENTS IN RELATION WITH SYMPTOM PRESENTATION

NCS PARAMETERS	NUMBER OF PATIENTS		
	BURN/TINGLE	NUMBNESS	BOTH
PURE MOTOR	0	4	3
PURE SENSORY	10	1	0
MIXED SENSORY MOTOR	43	13	17
PURE AXONAL	10	6	4
PURE DEMYELINATING	34	9	1
MIXED AXONAL DEMYELINATING	9	3	15
NORMAL	6	3	0

DISCUSSION

Peripheral neuropathy occurs as a result of several common and rare diseases. It can be heterogenous in etiology, diverse in pathology, and varied in severity. In our study, out of 100 patients with peripheral neuropathy, 57 were males and 43 were females (Graph 1). Mean age was 51.6±13.71. There were 67 subjects in the age group of 35 to 65 years (36 males and 31 females) (Graph 2, Table 1).

A study carried out in two regions of Italy[5] estimated the frequency of chronic symmetric symptomatic polyneuropathy in people over the age of 55 years. Around 8% of people met these diagnostic criteria for polyneuropathy and the most common condition associated with polyneuropathy was diabetes.

A study of prevalence in Bombay,[6] inferred that the prevalence of peripheral neuropathy was 2 - 4% and the most common diagnoses were carpal tunnel syndrome and diabetic peripheral neuropathy. In our study, the most common etiology was diabetes mellites. 55 out of 100 patients were diabetic patients, of which 38 were merely diabetic with no other known etiology promoting to their neuropathy and remaining 17 patients had multifactorial etiology including vitamin B_{12} deficiency/ vitamin D deficiency/ hypothyroidism (Table2).

Neuropathy is the main peripheral nervous system manifestation of chronic ethanol abuse, and its occurrence has been well documented. It is possibly the earliest associated neurologic complication of alcoholism and affects nearly 90% of chronic alcohol users.[7] The neuropathy can affect both small and large peripheral nerve fibers.

In a study by Julian T et al.,[8] the prevalence of peripheral neuropathy amongst chronic alcohol abusers was 46.3% (CI 35.7- 57.3%) when confirmed via nerve conduction studies. Alcohol-related peripheral neuropathy generally presents as a progressive, predominantly sensory axonal length-dependent neuropathy. In our study, 22 patients of peripheral neuropathy had an etiology of chronic alcoholism, out of which 7 had associated vitamin B_{12}deficiency (Table2).

Peripheral neuropathy is one of the consequences of vitamin B_{12} deficiency and it rapidly improves with supplementation in the initial stages. Prolonged deficiency can lead to irreversible nervous system damage.[9] The American Diabetes Association position statement on diabetic neuropathy has highlighted the importance of excluding vitamin B_{12} deficiency in patients with diabetic neuropathy.[10] Metformin was earlier considered the first-line of treatment for type 2 diabetes mellitus because of its effectiveness, safety and multiple metabolic and cardiovascular benefits.[11] Malabsorption of vitamin B_{12} is one of the reported side effects of long-term metformin treatment.[12] Different studies conducted on type 2 diabetic patients taking metformin have reported 5.8–33% vitamin B_{12} deficiency.[13,14] The results of a meta-analysis based on 29 studies with 8089 participants showed that patients receiving metformin therapy had odds ratio of 2.45 (95% CI 1.74–3.44, $p < 0.0001$) of developing vitamin B_{12} deficiency in comparison to the non-metformin users.[12] They concluded that vitamin B_{12} levels were lower in type 2 diabetic patients on metformin compared to those on other oral anti-diabetic drugs, but without significant deficiency.[15](Table 2)

In the literature, the prevalence of neuromuscular disorders in thyroid dysfunction varies between 20% and 80%.[16,17,18] Peripheral neuropathy may be caused by severe, long-term, untreated hypothyroidism. Although the association between hypothyroidism and peripheral neuropathy is not fully understood, it is known that hypothyroidism can cause fluid retention resulting in swollen tissues that exert pressure on peripheral nerves.[19,20]

Gupta N et al.,[21] suggested that peripheral and central neuropathy develops in patients of hypothyroidism at an early stage of disease and the electrophysiological investigations of such patients can help in timely detection and treatment of neurological disorders that occur due to thyroid hormone deficiency. Hypothyroidism has been reported to be associated with prolonged latency.[22]In our study, we observed 4 patients presenting with burning sensation of limbs secondary to hypothyroidism (Table 2).

CIDP, though a demyelinating polyneuropathy, is associated with a concomitant axonal loss attributed to the primary demyelinating process.[23,24] Thaisetthawatkul et al. emphasized the dispersion of the distal compound muscle action potential as a very sensitive diagnostic criterion for chronic inflammatory demyelinating polyneuropathy.[25] In this study we observed 3 patients with CIDP.

Clinically, AIDP presents with an acute, distal, symmetric, flaccid, weakness that usually starts in the lower extremities and has an ascending pattern as time progresses.[26] In AIDP, the most common target is the myelinated sheaths across the axon and within Schwann cells, leading to a decrease in conduction velocity.[27]

Concomitant involvement of a peripheral nervous system in dermatomyositis/ polymyositis has been known as neuromyositis which was first introduced by Senator in 1893.[28]Onder et al.[29]reported the neuropathic involvement in 8 patients diagnosed with DM/PM. In 2003, Seinturier et al.[30] did a retrospective study of 31 patients with inflammatory myositis and searched for any data of neurological involvement. They were able to identify 3 patients with neuro-myositis, suggesting that this feature could be underestimated. The presence of peripheral neuropathy in the presentation of inflammatory myopathies must be considered despite its rare presentation.[31] In our study, one case of autoimmune myositis, triggered by viral infection, presented as lower limb paraparesis associated with pain. Clinically, power deficit with normal sensory examination and normal reflexes were elicited. On further evaluation, he had normal NCS, mildly elevated CPK, CK-MB and strongly positive antiRO_{52} and antiSSA (Table 2).

A study similar to ours, by Shariff et al.,[32] evaluated the peripheral neuropathy in type 2 diabetes mellitus by clinical examination and NCS, to correlate them with risk factors. They concluded that DPN is a highly dependent neuropathy, with lower extremity nerves more involved. Diabetic neuropathy is proportional to duration of diabetes. Severity of diabetic neuropathy was positively relating with higher blood glucose level. Paresthesia's and burning feet were most common found symptoms. Abnormal tendon reflexes and deep sensory loss were most common found signs and distal symmetrical type of polyneuropathy was the most common.

CONCLUSION

Peripheral neuropathy is a neurological disorder with variable presentation and numerous etiologies. Most frequent presenting symptom was burning/ tingling sensation, followed by numbness. Most common etiology was diabetes mellitus, followed by chronic ethanol abuse. In our study, we inferred that patients with multiple etiologies of peripheral neuropathy had more severe findings on NCS. Majority of patients with mild symptoms were found to have only sensory demyelinating lesions on NCS, whereas severe neuropathic symptoms revealed mixed sensory motor involvement with axonal lesions on NCS.NCS is an essential tool in the evaluation of the peripheral nervous system, and is extremely helpful in determining the modality of nerve injury, motor or sensory, and severity of lesion, axonal or demyelinating. NCS is a reliable index in diagnosis, treatment and prognosis of peripheral neuropathy. Hence, clinical features and NCS will guide the clinician to assess the severity of peripheral neuropathy and promote better management of patients.

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