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The clinico-etiological profile of peripheral neuropathy: A study of 100 non-diabetic patients in a tertiary care hospital in eastern India

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ABSTRACT: Context: Very few systematic studies are available in Indian literature on peripheral neuropathy, a common yet diagnostically challenging disease in clinical practice. We conducted this clinical hospital-based study in eastern India over a period of seven years.

Aims: To study the epidemiological, clinical and electrophysiological profile of peripheral neuropathy in non-diabetic patients and to establish etiology as a final diagnosis of peripheral neuropathy.

Settings and Design: This was a prospective observational Hospital based study.

Methods and Material: The study comprises of peripheral neuropathy profile among 100 non diabetic patients of both sex and different age group ranging from 16 to 75 years attending neurology indoor and outdoor. All patients underwent detailed examination and serological-biochemical investigations, and electro-diagnostic studies. Cerebrospinal fluid examination and nerve biopsy were done as required

Statistical analysis used: Microsoft Excel

Results: Definitive diagnosis was reached in 75%cases (CIDP 18%, AIDP 16%, vasculitis 16%, Hansen's disease 9%, Hereditary neuropathy 8% and idiopathic 25%) Electrophysiological pattern of peripheral nerve involvement showed Demyelination in 37% , axonopathy in 31% , mixed in 24% , mononeuropathy multiplex in 8% and sensory neuronopathy in 9% cases. Nerve biopsy was done among 42 patients and 37 results were conclusive for the diagnoses.

Conclusions: Our study showed a relatively large number of vasculitis cases (16%). This may be due to our use of nerve biopsy in a substantial number of cases (42 out of 100). Etiology of 25% undiagnosed cases may be environmental toxins, autoimmune or rarer hereditary causes

Keywords: Peripheral neuropathy, Non-diabetic, Eastern India, Nerve Biopsy, Vasculitis

Key Messages:Peripheral neuropathy is a common neurological problem in clinical practice. Because of the variable presentation and disparate causes, a logical and sequential approach is necessary for the evaluation and proper management. Besides diabetes mellitus other etiologies are also prevalent in our community posing a diagnostic challenge.

I. INTRODUCTION

Peripheral neuropathies (PN) often present a challenge to the clinicians. After establishing its diagnosis, the etiopathology remains obscure in a considerable number of patients. In patients with initially undiagnosed peripheral neuropathy referred to specialized centres, a definite diagnosis can be made in more than 75% of cases.[1] Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) represents 13% to 20% of all initially undiagnosed neuropathies referred to specialized neuromuscular centers.[1] In our country, systematic studies related to the causes of peripheral neuropathy are very few in number.[2-4]

We had taken up a study in the Neurology Department of NRS Medical College, Kolkata which serve as a referral centre in West Bengal and also for other eastern Indian states and Bangladesh our neighbouring country. We excluded diabetic peripheral neuropathies (DPN) in our study for the following reasons: i) DPN cases are usually not admitted in indoor except in exceptional situations, ii) we tried to focus more on the challenging cases where diagnosis is unclear on the first presentation. DPN cases usually present little difficulty in diagnosis if studied systematically.

Our study is a prospective observational hospital-based clinical study which represents the etiological spectrum of PN in a large part of southern West Bengal and adjacent states in eastern India. The aims and objectives of this study are i) to study the epidemiological, clinical and electrophysiological profile of peripheral neuropathy in non-diabetic patients and ii) to establish etiology as a final diagnosis of peripheral neuropathy

II. SUBJECTS AND METHODS

The present study comprises of peripheral neuropathy profile among 100 non-diabetic patients of both sex and different age group ranging from 16 to 75 years attending neurology indoor and outdoor. This was a prospective observational study done in the neurology department of NRS Medical College from 2010-2017 after prior permission from institutional local ethical committee. Inclusion criteria were patients with lower motor neuron weakness or sensory symptoms along the distribution of single or multiple peripheral nerves with or without autonomic involvement. Pure motor weakness and pure sensory presentations were also included. Exclusion criteria were patients with diabetes mellitus [fasting blood sugar >110mg and post meal blood sugar >140mg], myopathy [by EMG and muscle enzymes], motor neurone disease or upper motor neuron lesions. All patients were admitted in the indoor for detail evaluation after they agreed to participate in this study by giving their written consent. A detailed history was taken regarding disease onset, duration, progression, clinical features, family history, and history of exposure to drugs and toxins, presence of associated systemic illness and thorough neurological examination. Patients had to fill a preformed questionnaire and were particularly inquired about the inciting factors like alcoholism, substance addiction, sexual promiscuity, metallic poisoning, occupational toxic exposures, alternate medicine use, Hansen's disease, syphilis and malignancy. Thorough neurological examination was done in every patient giving emphasis to sensory and autonomic examination. Vibration perception threshold was tested by tuning fork (128 Hz) and pain sensation was tested by pinprick, touch sensation by wisp of cotton, position sense and deep tendon reflexes were evaluated conventionally. In our study, peripheral neuropathy was diagnosed clinically with abnormal nerve conduction study (NCS) consistent with clinical presentation. Patients underwent the following investigations as indicated: complete blood count, sedimentation rate, blood biochemistry, vasculitic profile, HIV screening, serum vitamin B12, serum protein electrophoresis, CSF study and nerve biopsy after taking proper consent Electrophysiological studies including motor and sensory nerve conductions (NCS) of all four limbs and electromyogram (EMG) were the mainstay among all investigations. Reduced compound muscle action potential (CMAP) amplitudes with normal or near normal nerve conduction velocities with fibrillation in denervated muscles characterize axonal degeneration while the features of segmental demyelination include conduction block, reduced conduction velocities, prolonged distal latency and temporal dispersion. Neuropathy was divided into acute (<4 weeks), subacute (4-8 weeks) and chronic (>8 weeks) according to the duration of illness

III. RESULTS

Our study population was 100 patients of peripheral neuropathy. Men (n=70) were twice more affected than female (n=30). The mean age of presentation was 45 (range 16-75 years). The commonest pattern of presentation was between 1-12 months duration of illness [Figure -1]. The clinical features have been summarized in the [Table -1].

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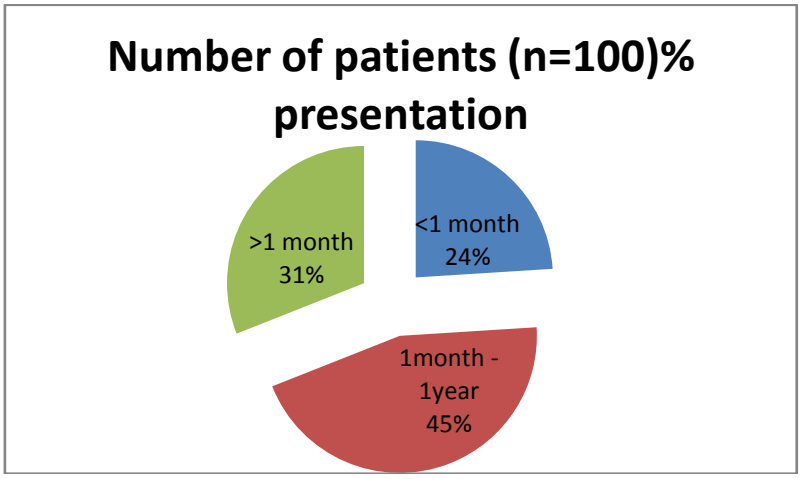

Figure – 1: Pattern of presentation of peripheral neuropathy in terms of duration of illness

Table 1: Clinical profile of peripheral neuropathy patients

Clinical presentation	Number of cases
Motor weakness Distal onset Upper limb onset	 75 18
Pure motor	24
Pure sensory	12
Sensory ataxia	29
Autonomic involvement	11
Cranial nerve involvement	15
Areflexia/hyporeflexia	91
Multiple mononeuropathy	11
Peripheral nerve thickening	31
Positive family history	5

Elctrophysiological pattern of peripheral nerve involvement according to NCS showed:
Demyelination: 37% , axonopathy: 31% , mixed: 24% , mononeuropathy multiplex: 8%, sensory neuronopathy :9%

Nerve biopsy was done among 42 patients and 37 results were conclusive for the diagnoses as follows: CIDP (n=14), Vasculitis (n=12), Hansen's disease (n=6) and hereditary motor sensory neuropathy (HMSN) (n=5)

Table 2 shows the comprehensive list where we could reach to a conclusive diagnosis based on clinico-electro-pathological tests. 75% of our study group were offered definite etiological diagnosis and prognosis. Five cases were related to drugs, two cases were proved to be paraneoplasticandetiopathological diagnosis remained still unknown in 25% cases of peripheral neuropathy [Figure 2].

Table 2: Etiology of different neuropathy cases

Neuropathies (Final etiological diagnosis)	 % distribution (n=100)
CIDP	18
Vasculitis	16
AIDP	 13
Hansen's	 9
HMSN	8
drugs/toxin	 5

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AMAN	2
paraneoplastic	2
MADSAM	1
MFS	1
Idiopathic	25

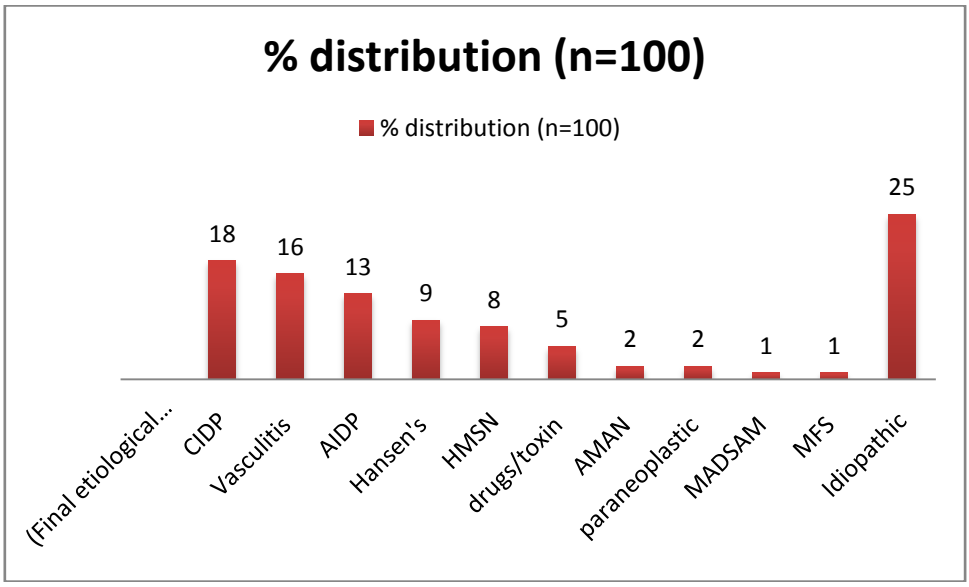

Figure 2: Etiology based distribution of non-diabetic peripheral neuropathy cases

IV. DISCUSSION

Peripheral neuropathy, though a common neurological disorder, is always a diagnostic and therapeutic challenge to the attending neurologist.[5] The reasons may be its wide clinical and etiological spectrum, a large number of investigations (sometimes invasive) needed and occasional need for long term follow up. We pooled our data from a medical college in Kolkata in West Bengal that serves as a tertiary care centre over a period of nearly seven years (2010 to 2017). The subject population represented a wide geographical area, mostly south Bengal and occasionally neighbouring Indian states and countries too. The geographical distribution and long period of observation have given the study a representative character in our consideration.

Large studies of this pattern are few in number all over India. Only one study, to our knowledge, has been carried out in West Bengal so far.[6] Another similar study from Bangladesh has been published recently.[7] Others available for comparison were conducted over a wide time span and geographical area and are also few in number.[5, 8-11]

We excluded diabetic neuropathy for two reasons, it is diagnosed with relative ease and usually these cases are not admitted indoor in our institution unless otherwise indicated. We wanted to focus on diagnostically challenging cases. One available study from Chandigarh is comparable to ours in this regard.[11] Other studies have a significant proportion of diabetic neuropathy ranging from 11% to 55% cases. [6,9]

Male: female ratio in our study was 70: 30 similar to other studies.[6,11] We feel this represents a bias inherent in a hospital based study.

The largest etiological group in our series comprised of CIDP (chronic inflammatory demyelinating polyneuropathy) – 18%. Other studies from Kolkata and Bangladesh had a share of 9% and 25% respectively when diabetes was excluded.[6-7] The study from Kashmir showed a share of 20% CIDP in nondiabetic cases, comparable to our study.[8]

The next most frequent causes were jointly vasculitis (16%) and Guillain Barre syndrome (16%) taking together Acute inflammatory demyelinating polyradiculoneuropathy (AIDP 13%), Acute motor axonal neuropathy (AMAN 2%) and Miller Fisher

syndrome (MFS 1%) . Interestingly only one study from Kolkata had cases of vasculitis, the share being 2.5% after exclusion of diabetes.[6] 14 out of 16 cases of vasculitis in our series were biopsy proven. We used nerve biopsy comparatively liberally (42 out of 100 cases) and this may be the reason for the diagnosis of a large number of cases as vasculitis.

Out of 42 biopsies, 37 yielded results. Apart from 14 cases diagnosed as vasculitis, 12 came out to be CIDP, 6 as Hansen's disease and 5 as hereditary neuropathies. All specimens were sent to NIMHANS- neuropathology department for histopathological examinations. One of the highlights of our study is the importance of nerve biopsy as a diagnostic tool in the study of peripheral neuropathy.

Various series in India showed the frequency of GBS from 16% to 46%.[6] Similarly, the studies compared to ours GBS ranged from 17% to 33%, after excluding diabetes, a slightly higher figure than ours. The lower figure in our study may be due to the admission of a large number of GBS cases in emergency medicine ward.

The fourth commonest cause was leprosy (9%). Leprosy as a cause ranged from 0 to22% in other studies after exclusion of diabetes.[8,11] Epidemiological variation and selection bias may be the probable reasons for such variability. However, two facts need to be highlighted here. One - leprosy still an important cause of peripheral neuropathy in India. Two – apart from high level of clinical suspicion, nerve biopsy may be necessary to establish the diagnosis, as is evident in our series where 6 out of 9 leprosy cases were biopsy proven.

Hereditary sensory motor neuropathy (HMSN), the fifth largest cause (8%), was comparable to other studies.[6,9] Slightly higher figure in ours may reflect referral bias.

Drugs and toxins accounted for 5% cases compared to 8.5% and 5% in the studies from Kolkata and Bangladesh respectively. Two cases were related to drugs (methotrexate) and three cases to alcohol abuse. Only one case of multifocal acquired demyelinating sensory and motor polyneuropathy (MADSAM) and two cases of paraneoplastic neuropathies were the rarer varieties. The later had association with colonic adenocarcinoma and penile CA.

The idiopathic group where no cause could be found comprised of 25%. The reference studies had a comparable figure in non-diabetic cases (19% to 25%).[6,9] In our opinion autoimmune, toxic or rarer hereditary causes may be responsible for such undiagnosed cases, the share of which remains fairly constant over a wide geo-social distribution.

Infrastructural paucity, lack of facility for long term follow up and our present lack of understanding of the disease process are some of the factors responsible for the current scenario.

Limitations of this study are lack of metabolic causes (other than diabetes) e.g. CRF, endocrine or hepatic as they are usually managed by other departments. Environmental toxins e.g. arsenic and heavy metals are important causes of neurotoxicity in Gangetic West Bengal, but they were not adequately represented in the current study. We strongly feel the need of a large, adequately controlled, epidemiologic study to properly evaluate the role of toxic environmental agents causing neuropathy and other neurological disorders.

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