



4-2010

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## Recommended Citation

Sher, K.; Firdaus, H; and Ali, S (2010) "Spectrum of Chronic Acquired Immune Neuropathies," *Pakistan Journal of Neurological Sciences (PJNS)*: Vol. 5 : Iss. 1 , Article 3.

Available at: <https://ecommons.aku.edu/pjns/vol5/iss1/3>

# SPECTRUM OF CHRONIC ACQUIRED IMMUNE NEUROPATHIES

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Pak J Neurol Sci 2010; 5(1): 6-9

## ABSTRACT

**Objective:** To determine the different clinical presentations of patients with acquired immune mediated neuropathies. **Methodology:** This was a hospital based prospective study over a period of 2 years in a series of patients with electrophysiological evidence of chronic acquired immune neuropathies. **Results:** Males out-numbered females by 7 (19 vs 12). Majority of patients with chronic acquired immune neuropathies were found to have typical symmetric sensorimotor pattern with variable involvement of proximal and distal muscles. The sensory pattern was the next common pattern followed by asymmetric pattern consistent with madsaM neuropathy. **Conclusion:** Because immune mediated neuropathies are potentially treatable entities, it is essential to keep in mind their unusual presentations besides the typical symmetric pattern of weakness of limb girdle muscles.

## INTRODUCTION

Neuropathies are routinely classified as demyelinating or axonal, based on the presence or absence of demyelinating abnormalities on electrodiagnostic testing. The presence of conduction block/temporal dispersion reflects acquired nature of immune neuropathies and has been reported in patients with generalized, distal and asymmetric phenotypic pictures. Chronic acquired immune polyneuropathies are heterogeneous group of disorders, which may present in a variety of ways, besides the typical symmetric pattern observed in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). It is therefore important to appreciate different clinical presentations of underlying immune mediated neuropathies because majority of these are potentially treatable entities.

## MATERIAL AND METHODS

### *Place of study*

This study was carried out at Jinnah Post Graduate Medical Centre in Karachi over a period of 2 years from June 2006 to June 2008. This was a prospective clinical study.

### *Inclusion criteria*

All the adult male and female patients who presented with chronic proximal and/or distal weakness of more than one limbs in symmetric or asymmetric fashion were included in the study.

### *Exclusion criteria*

Any of the patients with one or more of the following features was excluded from the study:

- 1) History of diabetes mellitus, uremia, chronic liver disease or alcoholism.
- 2) Positive family history of similar illness.
- 3) Any patient with foot deformities, sphincter impairment, mutilation of hands and feet, ichthyosis, or retinitis pigmentosa.
- 4) History of drug or toxic exposure likely to cause neuropathy.

### *Methods*

Patients with chronic acquired neuropathies with neurophysiological features of segmental demyelination in any combination, i.e. conduction block (CB), slowing of conduction across the affected segment (proximal and/or distal), prolonged distal latency and/or temporal dispersion (TD) were evaluated over a period of 2 years. Those who

met revised neurophysiological criteria (Nicolas et al.) for CIDP were clinically categorized into different groups.

The following segments were considered for analysis: tibial (ankle and popliteal fossa), peroneal (ankle and below the fibular head), ulnar (wrist and below elbow), and median nerve (wrist and elbow). Electro diagnostic changes that were considered features of demyelination were similar to those proposed by American Academy of Neurology (AAN) committee (AAN, 2001), but with more stringent criteria for partial conduction block/temporal dispersion (NICOLAS ET AL). Revised neurophysiological criteria by Nicolas et al. were categorized into following four groups.

**GROUP 1:**

CB/TD must be present in one nerve and abnormal conduction values in at least two other nerves.

**GROUP 2:**

CB/TD must be present in two different nerves and abnormal conduction values in one other nerve.

**GROUP 3:**

CB/TD present in at least 3 different nerves with abnormal conduction values suggesting demyelination in at least one nerve including one of the nerves with CB/TD.

**GROUP 4:**

No CB/TD but abnormal conduction values must be present in three different nerves.

CSF Study was also performed in all the patients and those with CSF content of more than 100 mg/dl were categorized as having high protein content.

The muscle strength was measured manually in abductors of shoulders, flexors and extensors of neck, elbows, wrists, fingers, hips, ankles and toes by means of the Medical Research Council (MRC) scale.

Functional impairment was assessed with modified Rankin Disability scale:

- 0) Asymptomatic.
- 1) Non-Disabling symptoms that don't interfere with activities of daily living..
- 2) Slight Disability (unable to carry out all activities, such as running, but still able to look after themselves).
- 3) Moderate disability (but able to walk without assistance).
- 4) Moderately severe disability (unable to walk without assistance).
- 5) Severe Disability (Dependant)

For purpose of analysis patients with generalized (pattern) neuropathy were defined as having either symmetric proximal weakness or proximal plus distal weakness of major muscle groups.

Patients with distal pattern were defined as having symmetric distal large fiber sensory loss (Romberg's positive) or glove stocking numbness with or without distal weakness.

The asymmetric neuropathy was defined as having motor asymmetry, which differs by at least one grade in a minimum of 2 muscle groups, based on the MRC scale.

**RESULTS**

*1) Age and Sex*

Out of total 31 patients, 19 were males and 12 were females. Patients were categorized into different age groups where in majority were found between 40-60 years of age.

*2) Clinical Variant*

Of the 31 patients, majority of patients were found to have generalized pattern followed by distal pattern.

**TABLE 1.** Demographic details and distribution of various clinical variants of neuropathy in the sample population.

		Male n=19(%)	Female n=12(%)	Total n=31(%)
<b>Age</b>	Under 30	2(10.5%)	1(8.3%)	3(9.7%)
	30-39	5(26.3%)	2(16.7%)	7(22.6%)
	40-49	1(5.3%)	6(50.0%)	7(22.6%)
	50-59	8(42.1%)	2(16.7%)	10(32.3%)
	60 & above	3(15.8%)	1(8.3%)	4(12.9%)
<b>Clinical Variant</b>	CIDP	12(63.2%)	9(75.0%)	21(67.7%)
	MADSAM	1(5.3%)	1(8.3%)	2 (6.5)
	DADS	5(26.3%)	2(16.7%)	7(2.3%)
	MMCB	1 (2.3%)	0	1(13.2%)

*3) CSF Analysis*

CSF analysis revealed protein concentration of <100 mg/dl in majority of patients. Four out of 7 patients with distal pattern had CSF protein concentration >100 mg/dl.

*4) Weakness pattern in different Variants*

Out of 21 patients with generalized pattern, 10 has equally symmetric proximal as well as distal weakness followed by proximal > distal pattern. Patients with distal

pattern were found to be more ataxic rather than having glove and stocking sensory pattern.

5) *Functional state*

Majority of patients with generalized pattern were found to have moderate disability compared to distal pattern who were mainly found to have slight disability.

6) *Electro-diagnostic Criteria*

Patients with generalized pattern were found to have CB/TD in majority of cases (group 2 & 3). CB/TD was infrequent with distal pattern of CIDP.

**DISCUSSION**

CIDP is a clinically heterogeneous group of polyneuropathies united by their presumed immune mediated etiopathogenesis. In clinical practice, it is unusual to take into consideration different clinical phenotypes of CIDP while coming across patients with neuropathic symptoms. However distinction between these subgroups is of immediate practical relevance to patient management.<sup>2</sup> The disorders, which have some characteristics unique but otherwise have clinical, electrophysiologic, laboratory and therapeutic aspects similar to CIDP, are considered variants.<sup>1</sup>

Since the first consensus criteria proposed by the American Academy of Neurology in 1991, numerous authors have proposed alternative ones.<sup>10</sup> However as there is no gold standard parameter for diagnosis of CIDP, we selected the proposed revised electrophysiological criteria by Nicolas et al. for diagnostic purpose.<sup>5</sup>

The disease is believed to more likely affect all age groups but is more common in older males.<sup>7</sup> Our study found similar pattern wherein 21/31 patients were above 40 at the time of diagnosis. CIDP is traditionally distinguished from chronic length dependent polyneuropathies by uniform muscle weakness (proximal as well as distal) of upper and lower limb with generalized areflexia.<sup>10</sup>

Similar pattern of global weakness of upper and lower limbs was noticed in majority of our patients (32%) followed by proximal more than distal (22.6%) and then distal more than proximal (12%) patterns. Thus it is important to keep in mind that predominant proximal or distal weakness with hyporeflexia or areflexia with or without sensory symptoms may be presenting patterns of CIDP.

As CIDP is heterogeneous in presentation with unusual patterns like ataxic and distal asymmetric variants,<sup>8</sup> we also came across such patterns in our series of patients. Typically a pure or predominant sensory presentation have also been reported to occur in presence of marked motor nerve slowing with relative preservation of motor function. Our patients with DADS pattern were ataxic in 42% (3/7) of case whereas pure distal numbness was found in 28% (2/7) of cases. One patient in this group was found to have more distal sensory motor involvement of hands than feet.

Two out of thirty patients were found to have distal asymmetric pattern, proportion corresponding to series of patients studied by M. Bushby et al.<sup>2</sup>

**TABLE 2.** Clinical spectrum of various neuropathies

		<b>CIDP</b> n=21	<b>MADSAM</b> n=2	<b>DADS</b> n=7	<b>MMCB</b> n=1
<b>Distribution of Weakness</b>	Proximal= Distal (P=D)	10 (47.6%)			
	Proximal> Distal (P>D)	6 (28.6%)		1(14%)	
	Distal Ataxic			3(43%)	
	Distal Numbness			2(29%)	
	Asymmetric (D/P)		2(100%)		
	Distal> Proximal (D>P)	5(23.8%)			
<b>Functional Status</b>	Distal (UL)			1(14%)	1(100%)
	Slight disability (grade 2)	9(42.9%)	1(50%)	5(71%)	1(100%)
	Moderate disability (grade 3)	10 (47.6%)	1(50%)	2(29%)	
<b>Electro Diagnostic Criteria (Nicolas et al.)</b>	Severe Disability (grade 4)	2(2.5%)			
	Grade 1		1(50%)		
	Grade 2	6(28.6%)	1(50%)		1(100%)
	Grade 3	6(28.6%)		6(86%)	
<b>CSF Protein (mg/l)</b>	Grade 4	3(14.3%)		1(14%)	
	Under 50	5(23.8%)	1(50%)	1(14%)	
	51-100	10(47.6%)		2(29%)	1(100%)
	>100	6(28.6%)	1(50%)	4(57%)	

CSF study was carried out in all patients and interestingly, the proportion of patient with protein content of more than 100 mg/dl was higher in those with DADS than in those with typical CIDP pattern. This needs further elucidation.

Because conduction block and temporal dispersion are highly suggestive of segmental demyelination, therefore we selected the proposed revised neurophysiological criteria by Nioles et al. which gives special emphasis to markers of demyelination.<sup>5</sup>

It came to our notice that patients with diffuse weakness were found to have increased proportion of patients with CB/TD than those with distal sensory or ataxic patterns. This observation suggests that all electrophysiologic features of demyelination are important to look for in diagnostic neurophysiologic studies.

The aim of this study was to enhance awareness about clinical profile of CIDP, which is usually considered uniform and symmetric neuropathic entity.

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