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Nerve Conduction Studies of Lower Limbs in Rheumatoid Arthritis Patients

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ABSTRACT:

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder which affects the joints and is associated with swelling, stiffness and pain. As RA causes functional limitations in the joints, this might affect the movements or the movement patterns of the damaged and inflamed joints. The prevalence of rheumatoid arthritis in India is about 1 to 1.5 %. The primary targets of inflammation are synovial membranes and articular structures but other organs also affected. Nerve conduction studies are most commonly used test, it is the main laboratory technique for the study of peripheral nerve function and it involve the surface stimulation of motor & sensory nerves. The result of these motor & sensory nerve conduction studies is expressed as amplitudes, latencies & conduction velocities. Aim and Objective: Nerve conduction Studies of Lower Limbs in Rheumatoid Arthritis Patients. Material and Methods: 50 Rheumatoid Arthritis patients and 50 controlled subjects were randomly selected. Patients from the Rheumatology OPD. Age group of the subject from 25 to 65 years and it includes both male & female. A complete NCS was done by using a NEURO -MEP - NET (NEUROSOFT) Machine according to standard protocol and settings. Nerves are tested on major affected side in all rheumatoid arthritis patients and unilaterally in control subjects. The electrodes used were of 3 types, i.e. active, reference and ground. Result: Comparison of the results of RA patient with healthy controls subject, both Motor and sensory nerve conduction studies in deep peroneal and sural nerve was prolonged latency, low amplitude and decreased conduction velocities. Conclusion: Abnormal electrophysiological findings existed more in rheumatoid arthritis patient than control group. This could be due to peripheral neuropathy in RA patients.

KEY WORDS: Rheumatoid arthritis (RA), Nerve Conduction Velocity (NCV), Nerve Conduction Studies (NCS), Latency (L), Amplitude (A), Action Potential (AP).

I. INTRODUCTION

Rheumatoid Arthritis is a chronic systemic disease of unknown etiology. It is characterized by peripheral symmetrical polyarthritis. It has a progressive course with exacerbation and remissions being part of its natural history. The prevalence of rheumatoid arthritis in India is about 1 to 1.5 % [11,12]. It begins with pain, stiffness and swelling of specific joints such as proximal interphalangeal, metacarpophalangeal, wrist and knee joints. The diagnosis is based routinely on the persistence of arthritic symptoms over a time. Important factors associated with RA are the possibility of infectious triggers, genetic predisposition and autoimmune responses. The primary targets of inflammation are synovial membranes and articular structures [3]. Rheumatoid arthritis (RA) is a chronic inflammatory disorder which affects the joints and is associated with swelling, stiffness and pain.

RA is diagnosed on clinical, serological and radiological grounds. The American Rheumatism Association (ARA) first proposed classification criteria for RA in 1956 and then revised them in 1958 ^[4,5]. As RA causes functional limitations in the joints, this might affect the movements or the movement patterns of the damaged and inflamed joints ^[7,8,9,10,11,12,13]. Nerve conduction studies is most commonly used test, it is the main laboratory technique for the study of peripheral nerve function and it involve the surface stimulation of motor & sensory nerves recording of the elicited action potential in muscle(CMAP) and the sensory nerve action potential (SNAP). The result of these motor & sensory nerve conduction studies is expressed as amplitudes, latencies & conduction velocities ^[14,15]





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Standardization and Quantification: Filter setting, type and size of electrode, location & recording of stimulating electrode, and measurement method should be defined. The recommended filter settings are 20-2000 Hzs pass bands for sensory nerve conduction studies and 20-10000 Hzs for motor conduction studies.

Aim and Objective: Nerve Conduction Studies of Lowe Limbs in Rheumatoid Arthritis Patients

Material and Methods: After clinical evaluation and laboratory investigation, those patients satisfying the Modified American Rheumatology Classification Criteria (1987) were included in the study. 50 Rheumatoid Arthritis patients and 50 controlled subjects were randomly selected from the Rheumatology OPD. Age group of the subject from 25 to 65 years and it includes both male & female.

Inclusion criteria: Diagnosed Rheumatoid Arthritis Patients Exclusion Criteria:

- Hemoglobin <10 gm/dl
- Pregnant Women
- Suffering from Diseases like diabetes mellitus, Parkinson's disease, cardiovascular diseases likes hypertension, ischaemic heart disease, congestive heart failure, valvular heart disease, cardio- myopathy and cardiac arrhythmia. Neurological diseases like multiple sclerosis, polyneuropathy or Guillain-Barre Syndrome.
- Drugs that interfered with the ANS including antihypertensive, diuretic, adrenergic inhibitor, anti-arrhythmic, sedative, hypnotic, epileptic drugs were also excluded from the study.

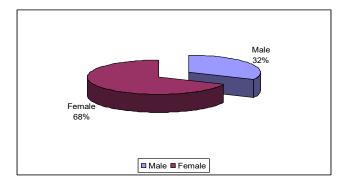
Procedure: An accessible nerve is stimulated through the skin by surface electrode, using a stimulus that is large enough to recruit all the nerve fiber. The resulting action potential is recorded by electrode on skin:

- 1. Over the muscle (belly-tendon electrode) in case of motor fibers stimulated in a mixed or motor nerve (CMAP).
- 2. In orthodromic conduction: a distal portion of nerve e.g. digital nerve is stimulated and sensory nerve action potential (SNAP) is recorded at a proximal point along the nerve. In antidromic conduction: the nerve is stimulated at proximal point, and action potential is recorded distally.

Instruments Used: NEURO – MEP – NET

II. RESULT AND DISCUSSION

Graph 1: Gender Distribution of RA Patients:



The present study had 16 males accounting for 32 % and 34 females accounting for 68 %. (NEUROSOFT) (8 channel)



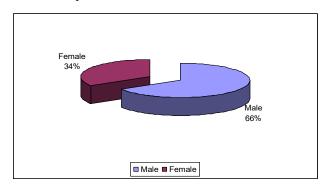


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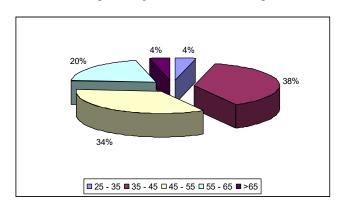
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Graph 2: Gender Distribution of Controls



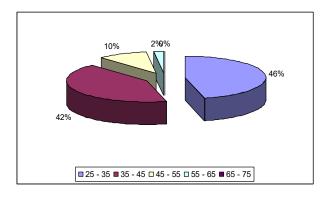
The present study had 33 males accounting for 66 % and 17 females accounting for 34

Graph 3: Age Distribution of RA patient



The maximum number of RA patients 19 (38%) was present in the age group of 35-45 years.

Graph 4: Age distribution of Controls



The maximum number of controls 23 (46%) was present in the age group of 25 - 35 years.





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Table 1: Finding of motor nerves

	Group	N	Mean ± SD	Unpaired t t	red t test	
Deep	peroneal					
nerve						
L	RA	50	10.20 ± 2.071	2.710	98	0.008
	Control	50	9.15 ± 1.820			
A	RA	50	4.39 ± 1.649	-3.159	98	0.002
	Control	50	6.21 ± 3.736			
CV	RA	50	49.55 ± 5.062	-5.795	98	0.000
	Control	50	57.86 ± 8.783			

P < 0.001 = highly significant, P > 0.001 to < 0.05 = significant, P > 0.05 = not significant.

Mean latency of motor deep peroneal nerve in RA patients was 10.20 ± 2.07 ms and 9.15 ± 1.82 ms for controls. There was statistically significant difference between the latency of RA patients and controls (p=0.008).

Mean amplitude of motor deep peroneal nerve in RA patients was 4.39 ± 1.64 mV and 6.21 ± 3.73 mV for controls. There was statistically significant difference between the amplitude of RA patients and controls (p=0.002).

Mean Conduction velocity of motor deep peroneal nerve in RA patients was 49.55 ± 5.06 m/s and 57.86 ± 8.78 m/s for controls. There was highly significant difference between the Conduction velocity of RA patients and controls (p=0.000).

Table 2: Finding of sensory nerves

	Group	N	Mean ± SD	Unpaired t test		
Deep per	roneal nerve					
L	RA	50	1.96 ± 0.55	-0.470	97	0.325
	Control	50	1.85 ± 0.57			
A	RA	50	25.43 ± 7.092	-0.719	98	0.474
	Control	50	27.37 ± 8.268			
CV	RA	50	51.08 ± 11.52	-1.055	98	0.294
	Control	50	55.97 ± 9.97			
Sural nei	rve					
L	RA	50	2.63 ± 1.35	-0.484	98	0.630
	Control	50	2.73 ± 0.67			
A	RA	50	17.78 ± 4.97	-0.487	98	0.627
	Control	50	18.34 ± 6.37			
CV	RA	50	54.59 ± 18.08	0.360	98	0.720
	Control	50	53.55 ± 9.60			

P < 0.001 = highly significant, P > 0.001 to < 0.05 = significant. P > 0.05 = not significant. Mean latency of sensory deep peroneal nerve in RA patients was $1.96 \pm 0.55 \,\mu\text{V}$ and $1.85 \pm 0.571 \,\mu\text{V}$ for controls. There was not statistically significant difference between the Conduction velocity of RA patients and controls (p=0.325).





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Mean Amplitude of sensory deep peroneal Nerve in RA patients was $25.43 \pm 7.09 \,\mu\text{V}$ and $27.37 \pm 8.268 \,\mu\text{V}$ for controls. There was not statistically significant difference between the Amplitude of RA patients and controls (p=0.474).

Mean Conduction velocity of sensory deep peroneal Nerve in RA patients was 51.08 ± 11.52 m/s and 55.97 ± 9.9 m/s for controls. There was not statistically significant difference between the Conduction velocity of RA patients and controls (p=0.294).

Mean latency of sensory sural Nerve in RA patients was 2.63 ± 1.35 ms and 2.73 ± 0.67 ms for controls. There was not statistically significant difference between the Latency of RA patients and controls (p=0.630).

Mean Amplitude of sensory sural Nerve in RA patients was $17.78 \pm 4.97 \,\mu\text{V}$ and $18.34 \pm 6.37 \,\mu\text{V}$ for controls. There was not statistically significant difference between the Amplitude of RA patients and controls (p=0.627).

Mean Conduction velocity of sensory sural Nerve in RA patients was 54.59 ± 18.08 m/s and 53.55 ± 9.6 m/s for controls. There was not statistically significant difference between the Conduction velocity of RA patients and controls (p=0.720).

Group RAControl Total L 48 96 N Count 48 % within 96.0% 96.0% 96.0% Group AN 2 2 4 Count % within 4.0% 4.0% 4.0% Group Total Count 50 50 100 % within 100.0% 100.0% 100.0%

Table 3: Deep Peroneal Nerve (Motor) – Latency

N= Normal, AN= Abnormal

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	0.000^{a}	1	1.000	
Fisher's Exact Test				1.000

Group

Latency of the motor deep peroneal nerve was abnormal in 2 (4%) of RA patients and 2 (4%) in controls and it was normal in 48 (96%) of RA patients and 48 (96%) of controls. There was not statistically significant difference between the abnormal latency of RA patients and controls (p=1.000).

Table 4: Deep Peroneal Nerve (Motor) – amplitude

			Group		
			RA	Control	Total
A	AN	Count	10	3	13
		% within Group	20.0%	6.0%	13.0%





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	N	Count	40	47	87
		% within Group	80.0%	94.0%	87.0%
To	tal	Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

N= Normal, AN= Abnormal

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	4.332 ^a	1	0.037	
Fisher's Exact Test				0.071

Amplitude of the motor deep peroneal nerve was abnormal in 10 (20%) of RA patients and 3 (6%) in controls and it was normal in 40 (80%) of RA patients and 47 (94%) of controls. There was statistically significant difference between the abnormal amplitude of RA patients and controls (p=0.037)

Table 5: Deep Peroneal Nerve (Motor) – conduction velocity

			Group		
			RA	Control	Total
CV	AN	Count	2	0	2
		% within Group	4.0%	0.0%	2.0%
	N	Count	48	50	98
		% within Group	96.0%	100.0%	98.0%
Tot	al	Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

N= Normal, AN= Abnormal

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	2.041 ^a	1	0.153	
Fisher's Exact Test				0.495

Conduction velocity of the motor deep peroneal nerve was abnormal in 2 (4%) of RA patients and 0 (0%) in controls and it was normal in 48 (96%) of RA patients and all controls. There was not statistically significant difference between the abnormal Conduction velocity of RA patients and controls (p=0.153).

Table 6: Deep Peroneal Nerve (sensory) – Latency

			Group		
			RA	Control	Total
L	N	Count	50	50	100
		% within Group	100.0%	100.0%	100.0%
Total		Count	50	50	100





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				Group		
			RA	Control	Total	
L	N	Count	50	50	100	
		% within Group	100.0%	100.0%	100.0%	
Total	<u> </u>	Count	50	50	100	
		% within Group	100.0%	100.0%	100.0%	

N= Normal, AN= Abnormal

Latency of the sensory deep peroneal Nerve was normal in both RA patients 50 (100%) and controls 50 (100%).

Table 7: Deep Peroneal Nerve (sensory) – Amplitude

				Group		
			RA	Control	Total	
A	AN	Count	7	10	17	
		% within Group	14.0%	20.0%	17.0%	
	N	Count	43	40	83	
		% within Group	86.0%	80.0%	83.0%	
Tot	al	Count	50	50	100	
		% within Group	100.0%	100.0%	100.0%	

N= Normal, AN= Abnormal

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	5.482 ^a	1	0.119	
Fisher's Exact Test				0.134

Amplitude of the sensory deep peroneal Nerve was abnormal in 7 (14%) of RA patients and 10 (20%) in controls and it was normal in 43 (86%) of RA patients and 40 (80%) of controls. There was not statistically significant difference between the abnormal Amplitude of RA patients and controls (p=0.119).

Table 8: Deep Peroneal Nerve (sensory) – Conduction velocity

			G	roup	
			RA	Control	Total
CV	AN	Count	3	0	3
		% within Group	6.0%	0.0%	3.0%
	N	Count	47	50	97
		% within Group	94.0%	100.0%	97.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

N= Normal, AN= Abnormal





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	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	3.093 ^a	1	0.079	
Fisher's Exact Test				0.242

Conduction velocity of the sensory deep peroneal Nerve was abnormal in 3 (6%) of RA patients and 0 (0%) in controls and it was normal in 47 (94%) of RA patients and all controls. There was not statistically significant difference between the Conduction velocity of RA patients and controls (p=0.079).

Table 9: Sural Nerve (sensory) – Latency

			G	Group		
			RA	Control	Total	
L	AN	Count	3	1	96	
		% within Group	6.0%	2.0%	96.0%	
	N	Count	47	49	4	
		% within Group	94.0%	98.0%	4.0%	
Total		Count	50	50	100	
		% within Group	100.0%	100.0%	100.0%	

N= Normal, AN= Abnormal

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	1.042 ^a	1	0.307	
Fisher's Exact Test				0.617

Latency of the sensory sural Nerve was abnormal in 3 (6%) of RA patients and 1 (2%) in controls and it was normal in 47 (94%) of RA patients and 49 (98%) of controls. There was not statistically significant difference between the abnormal Latency of RA patients and controls (p=0.307).

Table 10: Sural Nerve (sensory) – Amplitude

			G	roup	
			RA	CONTROL	Total
A	AN	Count	5	5	10
		% within Group	10.0%	10.0%	10.0%
	N	Count	45	45	90
		% within Group	90.0%	90.0%	90.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

N= Normal, AN= Abnormal





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	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	0.000^{a}	1	1.000	
Fisher's Exact Test				1.000

Amplitude of the sensory sural Nerve was abnormal in RA patients as well as controls 5 (10%) and it was normal in patients as well as of controls 45 (90%). There was not statistically significant difference between the Amplitude of RA patients and controls (p=1.000).

Table 11: Sural Nerve (sensory) – Conduction velocity

			G	Group		
			RA	Control	Total	
CV	AN	Count	3	0	3	
		% within Group	6.0%	0.0%	3.0%	
	N	Count	47	50	97	
		% within Group	94.0%	100.0%	97.0%	
Total		Count	50	50	100	
		% within Group	100.0%	100.0%	100.0%	

N= Normal, AN= Abnormal

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	3.093 ^a	1	0.079	
Fisher's Exact Test				0.242

Conduction velocity of the sensory sural Nerve was abnormal in 3 (6%) of RA patients and 0 (0%) in controls and it was normal in 47 (94%) of RA patients and in all controls. There was not statistically significant difference between the Conduction velocity of RA patients and controls (p=0.079).

Discussion:

Table 12: Motor nerves finding in present and previous study

Group				Geetanjali Sharma		Mc Combe PA	
		Present study		et al		et al	
		Mean ± SD	p-value	Mean ± SD	p-value	Range	p-value
Deep peroneal nerve							
L	RA	10.20 ± 2.071	0.008	10.1 ± 1.2	< 0.001	10.2	<0.001
	Control	9.15 ± 1.820		7.6 ± 0.8		2.9 - 5.6	
A	RA	4.39 ± 1.649	0.002	2.7 ± 1.3	< 0.001	<0.2	<0.001
	Control	6.21 ± 3.736		4.9 ± 1.1		2.5 - 14	





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CV	RA	49.55 ± 5.062	0.000	36.08 ± 3.3	< 0.001	22.5	< 0.001
	Control	57.86 ± 8.783		43.34 ± 2.1		41 - 56	

P < 0.001 = highly significant, P > 0.001 to < 0.05 = significant, P > 0.05 = not significant. L= Latency (ms), A= Amplitude (mV), CV= Conduction Velocity (m/s), SD= Standard deviation.

Table 13: Sensory nerves finding in present and previous study

Group		Due contested	4	Geetanjali Sharma et al	
		Present stu	dy	et ai	
		Mean \pm SD	p- value	Mean \pm SD	p- value
Deep	peroneal nerve				
L	RA	1.96 ± 0.550	0.325	-	-
	Control	1.85 ± 0.571			
A	RA	25.43 ± 7.092	0.474	_	-
	Control	26.60 ± 8.995			
CV	RA	51.08 ± 11.526	0.294	-	-
	Control	55.97 ± 9.979			
S	ural nerve				IF
L	RA	2.63 ± 1.358	0.630	4.88 ± 0.93	< 0.001
	Control	2.73 ± 0.670		3.4 ± 0.23	
A	RA	17.78 ± 4.973	0.627	0.184 ± 0.17	< 0.001
	Control	18.34 ± 6.373		0.33 ± 0.11	
CV	RA	54.59 ± 18.080	0.720	34.2 ± 7.2	< 0.001
	Control	53.55 ± 9.608		42.4 ± 1.2	

L= Latency (ms), A= Amplitude (μ V), CV= Conduction Velocity (m/s), SD= Standard deviation. P < 0.001 = highly significant, P > 0.001 to <0.05 = significant, P > 0.05 = not significant.

Electrophysiological Abnormality in previous study:

Monodeep Biswas at al [16]: in a study of peripheral neuropathy in RA patients found there were 29 patients (39.19%) who were diagnosed as having peripheral neuropathy after electro physiologic testing. Five patients (17.24%) had some clinical evidence of peripheral neuropathy. The other 24 patients (82.76%) had no clinical evidence of peripheral neuropathy. Fifteen (51.72%) patients with peripheral neuropathy had pure sensory neuropathy on the NCV study. Three patients (10.34%) had carpal tunnel syndrome. All the patients had axonal type of peripheral neuropathy and six patients (20.69%) had predominantly sensory impairment in the sensorimotor group of peripheral neuropathy and two patients (6.90%) had predominantly motor involvement. Geetanjali Sharma et al [17]: in electrophysiological evaluation of RA patients found, out of 25 patients of Rheumatoid arthritis, 6 had clinical evidence of peripheral neuropathy in the form of paraesthesia, loss of deep tendon reflexes and loss of vibration sense while remaining 19 subjects showed no clinical evidence of neuropathy. Ten patients showed mixed sensory motor neuropathy (40%) i.e. decrease in motor and sensory conduction velocity, slight increase in latency and markedly decrease amplitude of peroneal nerves. The decrease was more pronounced in lower limbs. Riyadh A. Sakini et al [18]: the electrophysiological studies revealed several forms of neuropathies in 35 RA patients, which accounted for 43.8% of neuropathic manifestations. Polyneuropathy and carpal tunnel syndrome were the relatively most common type of nerve involvement in rheumatoid arthritis, accounting for 22.8% of cases (8 of 35 cases) each. Further analysis of the data revealed that the association of polyneuropathy with rheumatoid arthritis occurred in 10% of cases (98 out of total 80 cases). There was no relationship between the duration of illness and the occurrence of neuropathy (r=-0.209,





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P>0.050). In fact, rheumatoid patients with a history of illness less than 5 years are more likely to be complicated by neuropathy.

Mohamed Saufi Awang et al [19], Nerve Conduction Study among Healthy Malaysians finding was the mean velocities for median and ulnar nerves both motor and sensory were: 54.71 ± 5.69 m/s (motor) and 54.04 ± 7.02 m/s (sensory) for the median nerve and 60.57 ± 5.00 m/s (motor) and 52.92 ± 5.89 m/s (sensory) for the ulnar nerve. The mean velocities for the common peroneal (motor) and sural (sensory) nerves were 50.73 ± 4.60 m/s and 47.97 ± 4.48 m/s respectively.

In present study, finding of (motor nerves) deep peroneal nerve were nearly comparable to the study of Geetanjali Sharma et al. And P.A. McCombe et al. There were significant differences in finding of RA patients and controls (p=<0.05) whereas in the study of Geetanjali Sharma et al and P.A. McCombe et al there was highly statistical significant difference between the finding of patients and controls (p=<0.001).

Geetanjali Sharma et al were studied sural sensory nerves. Finding of present study was not comparable to the study of Geetanjali Sharma et al. The present study had no statistical significant differences between the finding of RA patients and controls (p=>0.05) whereas, in the study of Geetanjali Sharma et al there was highly statistical significant difference (p=<0.001].

Present study had several practical limitations. The major weakness of the study was the lack of a pathological gold standard namely "nerve biopsy" studies to confirm our electrophysiological findings.

III. CONCLUSION

Motor Nerve Conduction Studies: In Rheumatoid arthritis patients, deep peroneal nerve, 2 (4%) had prolonged distal latency, 10 (20%) had low amplitude of CMAP and 2 (4%) had low conduction velocity. In controls, deep peroneal nerve, 2 (4%) had prolonged distal latency, 3 (6%) had low amplitude of CMAP and none had low conduction velocity. Sensory nerve conduction studies: In deep peroneal nerve, none had abnormal distal latency, 7 (14%) had low amplitude of CMAP and 3 (6%) had low conduction velocity. In sural nerve, 3 (6%) had prolonged distal latency, 5 (10%) had low amplitude of CMAP and 3 (6%) had low conduction velocity. In controls, deep peroneal nerve, none had abnormal distal latency, 10 (20%) had low amplitude of CMAP and none had low conduction velocity. In sural nerve, (2%) had abnormal distal latency, 5 (10%) had low amplitude of CMAP and none had low conduction velocity. The nerve conduction demonstrated decreased compound muscle action potential (CMAP) or sensory nerve action potential (SNAP) suggestive of Axonal changes while increased distal latency and delayed conduction velocities suggestive of Demyelinating changes in both motor and sensory nerves. Frequency of neuropathy was higher in the patients with RA when compared with the control group, and the difference was statistically significant (p<0.05)

In conclusion, abnormal electrophysiological findings existed more in rheumatoid arthritis patient than control group. According to this finding, we suggest that patients be investigated electro-physiologically despite the associated discomfort of testing. Clinical examination alone may fail to detect early peripheral neuropathy. Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest

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