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Peripheral Neuro Electrodiagnostic Abnormalities in Patients with Multiple Sclerosis: A Cross Sectional Study

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ABSTRACT

Background: Multiple sclerosis (MS) is known to affect essentially the central nervous system; however, peripheral nerve involvement, as an additional cause of disability, has been recently noticed.
Objectives: This study was aimed to perform detailed electrodiagnostic assessments in MS patients to evaluate peripheral nervous system involvement.
Materials and Methods: A total of eighty MS patients were evaluated for probable peripheral nerves involvement in a cross sectional study from August 2012 to August 2013.Patients with evidence of radiculopathy, diabetes, uremia, and anemia or cobalamin deficiency had been excluded. Clinical disability was ascertained by applying Expanded Disability Status Scale (EDSS) score. All electrodiagnostic assessment was performed by a single expert operator. Demographic parameters and paraclinical findings including MRI plaques were recorded. The data were analyzed in SPSS version 19applying the paired t-test and Mann-Whitney U test.
Results: The sural nerves showed the most consistent finding of abnormal conduction velocity (30%). The most frequent amplitude disturbance was observed in the peroneal nerves (10%). We did not find a significant association between abnormal findings and EDSS or MRI plaques (p<0.05). Patients with raised latency of the sensory nerves were younger than those with normal figures (p<0.05). Also, patients with prolonged disease were more likely to show peripheral nerve disturbances (p<0.05).
Conclusion: Peripheral nerve involvement was seen in MS patients, without significant relationship with physical disability and MRI plaques. On the other hand, disease duration, age and male gender were associated with peripheral nerve abnormalities.

Keywords: Electromyography; Multiple Sclerosis; Peripheral Nervous System

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Introduction

Multiple sclerosis (MS) is the most common inflammatory demyelinating disease and the most significant cause of disability in young adults. Its most important pathological finding is the plaques of the central nerve system, with distinct areas of the demyelination in white matter of the central nerve system and relative axonal preservation [1]. Tissue damage and neurological symptoms are supposed to be the results of immune mechanisms that target myelin antigens in the central nervous system (CNS) [2].

In addition to the involvement of the CNS, demyelination of the peripheral nerve system has been observed in 5% to 74% of patients that may be due to similar pathogenesis affecting both peripheral and central nerves system [3,4,5]. With nerve conduction studies (NCS), peripheral nerve lesion can be determined by nerve conduction velocity, distal latency, and amplitude of Compound Muscle Action Potential (CMAP) or Sensory Nerve Action Potential (SNAP). In this manner, the damage of the myelin sheet results in raised distal latency and decreased nerve conduction velocity, while decline in CMAP and SNAP amplitude represents axonal damage [6].

Because of a wide range of reported abnormalities, we aimed to investigate NCS changes of the peripheral nerves in MS patients with emphasis on the duration of disease, age and disability. Also, this study examined the relationship between peripheral nerve disturbance and MRI plaques, which has not been reported.

Materials and Methods

The proposal of this prospective cross sectional study was approved by the ethics committee of Mashhad University of Medical Sciences. We studied 88 MS patients who referred from the neurology clinic of Qaem hospital, Mashhad, Northern east of Iran since August 2012 to August 2013. The diagnosis was confirmed based on the 2010 McDonald MS Diagnostic Criteria. The patients were investigated for diabetes mellitus, anemia, uremia, vitamin B12 deficiency or rheumatologic diseases through laboratory tests. Individuals with above conditions or with a history of trauma or surgery in the limbs, neck and lumbar spine, also myopathic findings and evidence of radiculopathy or carpal tunnel syndrome in the electrodiagnostic tests were excluded from the study.

Ultimately, a total of 80 patients completed the study. Written informed consent was provided by each participant.

Their disabilities were assessed according to the Expanded Disability Status Scale (EDSS) score through a precise neurological examination and recorded. According to clinical course, the types of MS were determined: relapsing remitting (RR), secondary progressive (SP), primary progressive (PP), and progressive relapsing (PR). Demographic information such as age, gender, and duration of the disease was recorded. They were placed in three age related groups: under 30, 31 to 40, and more than 41 years old. Next, they underwent nerve conduction studies of the ulnar, median, tibial, peroneal and sural nerves on both sides by EMG/NCV system, (1 Nihon Kohden Neuropack S1 MEB 2300 A / in Japan). Also, the number of plaques and the involved areas of the brain and spinal cord were calculated based on Magnetic Resonance Imaging (MRI)s taken during the previous

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year. After data collection and entry, the statistical software SPSS-19 was used to analyze the data and the paired t-test and Mann-Whitney U test were applied to compare the significance of variables. P-value less than 0.05 were considered as the significant difference level.

Results

The sample comprised of 80 MS patients, 15 male (18.8%) and 65 female (81.2%). The mean age of the participants was 31±7.5 year. The most common age group was younger than 30 years (47.5%). The most common type was relapsing remitting (RR) with 91.5%, followed by PR and SP. Mean duration of the disease was 47.1±5.1 months.

The average number of MRI plaques was 6.6±3.1and mean EDSS score was 1.3±0.43.

The mean amplitude, latency, and velocity of the sensory and motor nerves of the upper and lower limbs have been presented in table 1.Accordingly, among upper limb nerves, the most frequent disturbance of latencies and amplitudes were related to the ulnar nerves (15% and 6.2%, respectively), and of velocity was detected in the median nerves (20% of the motor branches and 25% of the sensory branches). In the lower limbs, abnormal latencies and amplitudes of the motor nerves were more prevalent in the peroneal nerves (16.25% and 10%, retrospectively) and disturbance of velocity was more commonly presented in the tibial nerves (27.5%).

Table 1. Electrodiagnostic findings of the peripheral nerves among MS patients

		Motor nerve			Sensory nerve		
Nerve	Index	Mean ± SD	Normal range	The number of patients with abnormal finding (%)	Mean ± SD	Normal range	The number of patients with abnormal finding (%)
Median	Amplitude (µV)	6.3± 2.5	≥ 4.0	2 (2.5)	39.3 ± 18.1	≥20	4(5)
	Latency (ms)	4.2 ± 0.63	≤ 4.4	5(6.2)	3.1± 0.81	≤ 3.5	12 (15)
	Velocity (ms)	49± 5.6	≥ 49	16 (20)	51± 6.1	≥ 50	20 (25)
Ulnar	Amplitude (µV)	9.1 ± 1.8	≥ 7.0	5(6.2)	34.8 ± 18.2	≥17	2 (2.5)
	Latency (ms)	3.1± 0.6	≤ 3.3	12 (15)	2.9 ± 0.44	≤ 3.1	10 (12.5)
	Velocity (ms)	48.4 ± 6.7	≥ 49	12 (15)	57.1±8.2	≥ 50	18 (22.5)
Peroneal	Amplitude (µV)	3.9 ±1.1	≥ 3	8(10)	-		-
	Latency (ms)	5.7±1.09	≤ 6.5	13 (16.25)	-		-
	Velocity (m/s)	50.2 ± 9.1	≥ 44	20 (25)	-		-
Tibial	Amplitude (µV)	7.1± 3.6	≥ 4	4 (5)	-		-
	Latency (ms)	4.9 ±1.05	≤ 5.8	7 (8.7)	-		-
	Velocity (ms)	47.4±7.6	≥ 41	22 (27.5)	-		-
Sural	Amplitude (µV)	-		-	10.1±5.2	≥6	8 (10)
	Latency (ms)	-		-	4.1± 0.81	≤4.4	13 (16.2)
	Velocity (ms)	-		-	45.2 ± 7.1	≥ 40	24 (30)

SD=Standard Deviation. The normal values arequotedfrom the reference text book (6)

We also examined the relationship between electrodiagnostic findings and gender, duration of the disease, MRI plaques and EDSS scores; the results are shown in table 2 to 6. According to this, there was a significant gender differences in favor of women in the frequency of amplitude disturbances of the examined motor nerves. The other electrodiagnostic findings did not differs statistically in the different sexes (Table 2).

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Table 2. The relationship between gender and abnormal findings of the nerves

Nerve	Index	Males With abnormal motor test (%)	Females with abnormal motor test (%)	Fisher Exact Test *p-value*	Males with abnormal sensory test (%)	Females with abnormal sensory test (%)	Fisher Exact Test *p-value*
Median	Amplitude	0 (0)	2 (2.5)	0.002	1 (1.1)	4 (5)	0.001
	Latency	2 (2.5)	3 (3.7)	0.213	5(6.2)	7 (8.7)	0.168
	Velocity	6 (7.5)	10 (12.5)	0.412	8 (10)	12 (16)	0.107
Ulnar	Amplitude	1 (1.1)	4 (5)	0.001	0	2 (2.5)	0.002
	Latency	3 (3.7)	7 (8.7)	0.441	4 (5)	8 (10)	0.174
	Velocity	5(6.2)	7 (8.7)	0.301	7 (8.7)	11(13.75)	0.168
Tibial	Amplitude	0 (0)	4 (5)	<0.000	-	-	-
	Latency	2 (2.5)	5 (6.2)	0.558	-	-	-
	Velocity	10 (12.4)	12 (16)	0.174	-	-	-
Peroneal	Amplitude	2 (2.5)	6 (7.5)	0.023	-	-	-
	Latency	4(5)	9 (11.1)	0.168	-	-	-
	Velocity	12 (16)	8 (10)	0.107	-	-	-

Regarding age, the patients with and without abnormal amplitude of sensory and motor upper limb nerves was in similar ranges. The average ages of patients with normal and abnormal latency of all motor nerves were similar except for the ulnar and the tibial nerves. Among the sensory nerves, patients with abnormal latencies of the median, ulnar, and sural nerves were significantly younger than those with normal figures. The other abnormal parameters were not showed to be related to age (Table 3).

Table 3. The relationship between age and abnormal findings of the nerves

		Motor nerve		Sensory nerve	
Nerve	Electrodignostic finding	Mean age± SD years	T test *p-value*	Mean age± SD years	T test *p-value*
Median	Normal	29.8±6.5	0.764	31.7±7.4	0.033
	Abnormal	27.8± 5.5	-	26.5±5.5	-
Ulnar	Normal	32.1±6.3	0.016	32.3±6.3	0.002
	Abnormal	28±4.3	-	24.5±5.4	-
Peroneal	Normal	30.1±4.1	0.868	-	-
	Abnormal	29.8 ±6.5	-	-	-
Tibial	Normal	31.8±5.6	0.001	-	-
	Abnormal	27.3±3.91	-	-	-
Sural	Normal	-	-	31.4±7.8	0.016
	Abnormal	-	-	28.1±3.2	-

Furthermore, data analysis showed that the average period of the disease was similar among patients with normal and abnormal amplitudes. However, it was significantly higher in patients with the following findings: abnormal amplitude of the sural and sensory median, increased latency of the motor median, ulnar, tibial and peroneal nerves, and raised latency of the sensory median nerves. The average duration of disease in patients with abnormal velocity of the all nerves was significantly more than those with normal velocity, except for the sural, the sensory ulnar and the motor tibial nerves (Table 4).

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Table 4. The association between electrodiagnostic findings of motor nerves and duration of MS

		Motor nerve			Sensory nerve		
Nerve	**Index**	**Electrodiagnostic finding**	**Mean years of disease ± SD**	***p-value***	**Electrodiagnostic finding**	**Mean years of disease ± SD**	***p-value***
Median	Amplitude	Normal	5.8 ± 3.4	0.235	Normal	5.7 ± 3.3	0.026
		Abnormal	6.5 ± 2.5		Abnormal	6.4 ± 2.1	-
	Latency	Normal	5.4 ± 3.1	0.001	Normal	5.4 ± 3.2	<0.0001
		Abnormal	9.4 ± 3.1		Abnormal	9.1 ± 3.2	
	Velocity	Normal	4.1 ± 2.8	0.007	Normal	4.8 ± 3.2	0.008
		Abnormal	6.6 ± 3.3		Abnormal	6.1 ±2.3	
Ulnar	Amplitude	Normal	5.7 ± 3.3	0.033	Normal	5.8 ± 3.4	0.382
		Abnormal	7.1 ± 3.3		Abnormal	8.0	
	Latency	Normal	5.4 ± 3.3	0.041	Normal	5.7 ± 3.3	0.745
		Abnormal	8.1 ± 3.1		Abnormal	6.8 ± 3.4	
	Velocity	Normal	4 ± 2.2	0.002	Normal	5.3± 3.5	0.001
		Abnormal	6.8 ± 3.5		Abnormal	3.5 ± 1.5	
Peroneal	Amplitude	Normal	5.7 ± 3.4	0.237	Normal	-	-
		Abnormal	7.1 ± 3.3		Abnormal	-	
	Latency	Normal	5.5 ± 3.3	0.004	Normal	-	-
		Abnormal	8.2 ± 3.5		Abnormal	-	
	Velocity	Normal	4.9 ± 2.7	0.007	Normal	-	-
		Abnormal	6.7 ± 3.4		Abnormal	-	
Tibial	Amplitude	Normal	5.8 ± 3.4	0.23	Normal	-	-
		Abnormal	6.4 ±2.5		Abnormal	-	
	Latency	Normal	5.7 ± 3.3	0.03	Normal	-	-
		Abnormal	8.1 ± 2.3		Abnormal	-	
	Velocity	Normal	6.4 ± 3.3	0.201	Normal	-	-
		Abnormal	5.2 ± 3.1		Abnormal	-	
Sural	Amplitude	Normal	-	-	Normal	5.4 ± 3.1	<0.000
		Abnormal	-		Abnormal	10.1 ± 2.2	
	Latency	Normal	-	-	Normal	5.8 ±3.3	0.218
		Abnormal	-		Abnormal	6.4 ± 3.3	
	Velocity	Normal	-	-	Normal	6.5 ± 3.3	0.001
		Abnormal	-		Abnormal	4.8 ± 3.1	

SD=Standard Deviation

There was no relationship between electrodiagnostic findings and the average number of MRI plaques and mean EDSS score (Table 5 and 6).

Table 5. The association between electrodiagnostic findings and the number of MRI plaques in MS patients

	Motor nerve			Sensory nerve		
Nerve	**Electrodiagnostic finding**	**Mean number of plaques ± SD**	***p-value***	**Electrodiagnostic finding**	**Mean years of disease ± SD**	***p-value***
Median	Normal	6.3 ± 3.0	0.37	Normal	6.7 ± 3.1	0.188
	Abnormal	7.3 ± 3.4		Abnormal	3.7 ± 2.5	
Ulnar	Normal	6.2 ± 2.8	0.101	Normal	6.5 ± 3.1	0.121
	Abnormal	7.8 ± 3.6		Abnormal	10	
Peroneal	Normal	6.2 ± 2.7	0.98	Normal	-	-
	Abnormal	7.2 ± 3.3		Abnormal	-	
Tibial	Normal	6.3 ± 2.6	0.581	Normal	-	-
	Abnormal	6.9 ± 3.6		Abnormal	-	
Sural	Normal	-	-	Normal	6.7 ± 3.3	<0.0001
	Abnormal	-		Abnormal	5.2 ± 3.3	

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Table 6. Mean EDSS score and latencies of the sensory nerves

	Motor nerve			Sensory nerve		
Nerve	**Electrodiagnostic finding**	**Mean EDSS ± SD**	***p-value***	**Electrodiagnostic finding**	**Mean EDSS ± SD**	***p-value***
Median	Normal	0.57±1.4	0.586	Normal	0.4±1.4	0.115
	Abnormal	0.95±1.2		Abnormal	0.79±1	
Ulnar	Normal	0.4±1.2	0.519	Normal	0.4±1.5	0.37
	Abnormal	0.15±1.5		Abnormal	0.39±1	
Peroneal	Normal	0.7±1.5	0.192	Normal	-	-
	Abnormal	0.99±1.2		Abnormal	-	
Tibial	Normal	0.98±1.2	0.627	Normal	-	-
	Abnormal	0.86±1.2		Abnormal	-	
Sural	Normal	-	-	Normal	0.4±1.4	0.686
	Abnormal	-		Abnormal	0.2±1.2	

Discussion

The most common abnormality in this study was found in the NCV of the sural nerves (30%), followed by the tibial nerves (27.5%). The reported abnormalities of the peripheral nerves are various in the previous studies. For example, NCV abnormalities were reported in 29.4% of MS patients by Gartzenk *et al.* [7] and in only 5% by Misawa *et al.* [3]. In Shefner's study, 9 patients out of 14 showed normal amplitude and velocity [8]. In Pogonzelski's study, 74% of sufferers had at least one abnormality of the electrodiagnostic parameters that was not shown to be related to age, sex, and duration of the disease [5], while in our study some of the electrodiagnostic disturbances were seen in younger ages. In Ayromlu's study, abnormal amplitude (22.5%) and velocity of the motor nerves (33%) were common, while the frequency of abnormal velocity of the sensory nerves was not more common compared with the normal population [9].

In a study conducted by Anlar *et al.* the most common electrodiagnostic abnormality was low amplitude of ulnar and sural nerves that were detected in 16.5% of MS patients. Again, this research did not show any relationship between peripheral nerve disorders and MS signs, neurologic deficits and gender [10]. In contrast, the present study showed that abnormal amplitude of some of the peripheral nerves was seen more in male patients, while velocity and latency disturbances did not differ with gender. Besides, it was observed that the longer duration of MS disease, the higher the frequency of some abnormal findings, specially delayed latencies of all motor nerves and the sensory median nerve.

On the other hand, the amplitude disturbances in our study, did not accompany a higher number of MRI plaques. Also, the EDSS scores were not related to electrodiagnostic parameters. Hence, we did not find an association between peripheral nerve affection and disability related to MS. Sarova-Pinhas *et al.* also showed no relationship between NCS findings and disability among MS patients [11], to best of our knowledge, the present study is the only one that analyzed the correlation between MRI plaques and NCS abnormalities.

Altogether, peripheral nerve involvements have been reported to be between 5 to 74 percent in MS patients [3,5,7,9,10]. This wide range of frequency may be attributed to genetic diversity or different sample sizes and inclusion/exclusion criteria. In the other Iranian study (Ayromlu *et al.*), the frequency of abnormalities was near to our study [9], which may be explained by genetic factors or common environmental agents that affect

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both peripheral and central nervous system. These findings may support some aspect of currently proposed pathophysiology of MS disease. On the other hand, based on the aim of the studies, the results are different. For instance, the lowest figure (5%) represented only significant demyelinating polyneuropathy reported by Misawa *et al.* [3], while the highest figure (74%) belonged to the Pogonzelski's study, showed any subclinical lesions of the peripheral nervous system in MS [5]. Also, sample size may justify the different results. Anlar *et al.*' study with 20 subjects reported 16.5% abnormalities, while Gartzen *et al.* study with a sample size similar to our study (54 subjects) found 29.6% abnormal findings [7].

In general, it seems that younger patients suffering from MS for longer periods of time are more susceptible to develop some peripheral nerve disorders, especially for delayed latencies of the motor ulnar and tibial, and the sensory median nerves. In addition, the presence of peripheral nerve abnormalities in some MS patients may open a window to understanding the nature of the demyelinating process in this disease.

Conclusion

This study showed that abnormalities of the peripheral nerve system occurred regardless of MRI plaques or EDSS. On the other hand, disease duration, age and gender were associated with some peripheral nerve abnormalities.

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Conflict of Interest

The authors have no conflict of interest.

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