

NERVE CONDUCTION STUDY AND ELECTROMYOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS

By

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ABSTRACT

Background: Standard neurological examination was found to be inadequate for diagnosing suspected early peripheral neuropathy in patients with Rheumatoid Arthritis (RA) though electrophysiological testing can be utilized for early diagnosis and defining the extent of peripheral nerve involvement.

Objective: To evaluate nerve conduction study and electromyography in patients with rheumatoid arthritis complained of neuropathic symptoms.

Patients and Methods: This study was carried out on thirty patients with clinical diagnosis of rheumatoid arthritis who had neuropathic symptoms as tingling or burning sensation in any extremity. Also control group consisted of thirty patients with clinical diagnosis of rheumatoid arthritis without evidence of peripheral neuropathy by history and examination. patient group subdivided into subgroup A (patients had neuropathic affection in nerve conduction study (NCS) and subgroup B (patient had normal findings in NCS).

Results: There was a highly statistically significant difference between patient and control groups as regarding neurophysiological evidence of neuropathy. There was a statistically significant difference between sub groups A and B as regarding age of the patients. There was also a highly statistically significant difference between sub groups A and B as regarding abnormal findings in clinical examination.

Conclusion: Possibility of presence of peripheral neuropathy in electrophysiological study in patients with rheumatoid arthritis who complained neuropathic symptoms was more than patients who didn't complain. Electrophysiological studies should be included in the routine examination of rheumatoid arthritis patients for early detection of neurological involvement

Key words: Rheumatoid arthritis, peripheral neuropathy, nerve conduction study, electromyography.

INTRODUCTION

Rheumatoid arthritis (RA) is a multisystem autoimmune disorder characterized by chronic deforming arthritis of predominantly small and large joints along with extra-articular manifestations such as interstitial lung disease, rheumatoid nodules, ophthalmic involvement like scleritis, vasculitis, and

neurological manifestations including various forms of peripheral neuropathy (*Van Oosterhout et al., 2008 and Karatoprak et al., 2013*).

Peripheral neuropathy in patients with rheumatoid arthritis presents in the form of mononeuritis multiplex, distal sensory, distal sensorimotor neuropathy, and

entrapment neuropathy (*Suppiah et al., 2011 and Makol et al., 2014*).

Clinical neuropathy may present with a wide variety of symptoms such as pain, paresthesia, and muscle weakness. These symptoms may mimic and overlap those of arthritis. It is often difficult to diagnose the presence of peripheral neuropathy if slight or early particularly in presence of joint pain and limitation of movement (*Turresson et al., 2002 and Kinter et al., 2010*).

Early diagnosis of nerve involvement will help prompt and timely interventions with redirection of management to prevent permanent neurologic sequelae, improve quality of life and chances for long-term survival with less morbidity (*Sherifa et al., 2005*).

In electromyography (EMG), electrical potentials are detected by a needle electrode inserted directly into a skeletal muscle. It assists in clinical diagnosis, prognosis and clinical management decisions. It is helpful in distinguishing between inflammatory, chronic, metabolic or inherited muscle diseases, and differentiating between acute, recovering and chronic denervation (*Lyell and Jones, 2012*).

Nerve conduction study (NCS) provides information regarding the presence, severity and location of a peripheral neuropathy, mononeuropathy, or disorders affecting the neuromuscular junctions. The functional modality most involved are sensory or motor, and the predominant pattern of pathology (*England et al., 2005 and Rubin, 2012*). Electrodiagnostic studies of mononeuritis multiplex show multifocal sensory motor

axonal neuropathy (*Campellone and Joseph, 2016*).

The aim of the present study was to evaluate nerve conduction study and electromyography in patients with rheumatoid arthritis complained of neuropathic symptoms.

SUBJECTS AND METHODS

Thirty patients with clinical diagnosis of rheumatoid arthritis, who had neuropathic symptoms as tingling or burning sensation in any extremity, were involved to study, and a control group consisted of thirty patients with clinical diagnosis of rheumatoid arthritis without evidence of peripheral neuropathy by history and examination. All patients attended the rheumatology clinic or admitted in the Department of Rheumatology, Al-Azhar University Hospitals (Al-Hussien & Bab El-Shaaria, in between November 2015 and May 2016. All patients met the American College of Rheumatology criteria for RA (*Sim et al., 2014*). Patient group was subdivided into subgroup A (14 patients had neuropathic affection in NCS) and subgroup B (16 patients had normal findings in NCS). Informed consent was obtained from all patients before the study.

Inclusion criteria: Patients had RA who were diagnosed and classified in the Department of Rheumatology at Al-Azhar University Hospitals, complained of neuropathic symptoms as tingling, numbness and weakness, and aged >18 years.

Exclusion criteria: Patients with systemic diseases (i.e., diabetes mellitus, hypo or hyperthyroidism, amyloidosis, liver failure, chronic renal failure or SLE), patients

who underwent orthopedic surgery, patients with neurologic disorders (i.e., GBS, transverse myelitis or MS), or pregnant women.

This study was a case-control study to:

1) Compare between presence of neuropathy in patients with RA who complained of neuropathic symptoms and others without neuropathic symptoms. 2) Determine the types and nature of neuropathy in patients with RA .

All patients in this study were subjected to: Full history: (personal history, family history, past history and full history of rheumatoid arthritis), *history of present illness*(motor system i.e. distal or proximal weakness, tone and muscle wasting, gait), *sensory system*, (i.e. tingling, numbness, deep sensory loss), and autonomic manifestation, i.e. impotence, hyper/anhydrosis, skin changes in LLS, postural hypotension, and sphincteric dysfunction).

Neurological examination: Motor system examination, (i.e . detection of wasting, fasciculation, tenderness and muscle power), sensory system examination, (i.e. superficial sensation, stock and glove hypoesthesia , deep sensation, Phalen's sign test, Tinels sign test), and autonomic systems i.e. cold extremities, skin changes, postural hypotension.

Joints were examined with special attention to: number of swollen joints and joint tenderness.

The functional status of patients with RA had been classified as class I–IV according to the revised criteria for the classification of the functional status in RA. A higher class reflects a poorer functional status (*Aletaha et al., 2010*).

Neuropathic symptoms and signs had been quantified with the neuropathy symptom score (NSS). The NSS is a five-question multiple-choice self-report inventory that is used for measuring the severity of neuropathic symptoms and signs. The NSS has a maximum score of 9, with a higher score indicating more severe neuropathic symptoms (*Sim et al., 2014*).

Electrophysiological study was done for both groups in Neurology Department, Al-Azhar University Hospitals. The skin temperature was kept between 31°C – and 32°C (*Sim et al., 2014*).

Motor nerve conduction was performed on the median, ulnar, peroneal and posterior tibial nerves with comment on distal latency, amplitude, duration and conduction velocity. F-waves were performed with comment on persistence and latency. Sensory nerve conduction was performed on the median, ulnar, superficial peroneal and sural nerves with comment on latency and amplitude. Sensory nerve conduction was studied antidromically.

Statistical analysis: Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. Qualitative data were presented as number and percentages, while quantitative data were presented as mean, standard deviations and ranges. The comparison between two groups with qualitative data were done by using *Chi-square test*. The comparison between two groups regarding quantitative data with parametric distribution was done by using *Independent t-test*. So, the p-value was considered significant when P was > 0.05.

RESULTS

This study was carried out on thirty patients (**patient group**) with clinical diagnosis of rheumatoid arthritis who had neuropathic symptoms as tingling or burning sensation in any extremity, **24 (80%) females, and 6 (20%) males**, and their ages ranged from **21 to 54** years with a mean of **34.10 ± 9.33 Table(1)** . and thirty patients (**control group**) with clinical diagnosis of rheumatoid arthritis without evidence of peripheral neuropathy by history and examination, **23(76.7%) females, and 7 (23.3%)males**, and their ages ranged from **22 to 56** years with a mean of **33.90 ± 8.76 (Table 1)**. In the present study, there was 14 patients had neuropathy by nerve conduction study and electromyography in patient group (46.7%), while there were 2 patients had neuropathy in control group. There was a highly statistically significant difference between patient and control groups as regarding neurophysiological evidence of neuropathy ($p < 0.01$ - **Figure 1**). *In patient group, as regarding type of neuropathy*, there was 8 patients had entrapment neuropathy (**57.14%**), three of them had bilateral Carpal Tunnel Syndrome (CTS), four of them had unilateral CTS, and only one patient had ulnar entrapment neuropathy. Two patients had mononeuritis multiplex (**14.29%**) affecting mainly peroneal and ulnar or peroneal and median nerves. One patient had mononeuritis simplex (**7.14%**) affecting superficial peroneal nerve (purely sensory). Three patients had polyneuropathy (**21.43%**), one of them (**7.14%**) affecting the nerves of both lower limbs, and two of them (**14.29%**)

affecting all nerves of upper and lower limbs (**Table 2**). *As regarding nature of neuropathy*, there was eight patients (**57.14%**) had demyelinating neuropathy, 7 patients (**50%**) of entrapment, and one patient (**7.14%**) had mononeuritis simplex. Four patients (**28.57%**) had axonal neuropathy two of them (**14.29%**) who had mononeuroitis multiplex and another two patients (**14.29%**) had poly neuropathy. Two patients (**14.29%**) had mixed neuropathy (demyelinating with secondary axonal neuropathy), one of them had severe bilateral CTS, and the other had polyneuropathy (**Table 2**).

The mean age of sub group A was **38.14** years, while the mean age of sub group B was **30.56 years** . Eleven patients in sub group A had positive family history, while in sub group B was 8. There was a statistically significant difference between sub groups A and B as regarding age ($p < 0.05$), while no statistically significant difference between sub groups A and B as regarding sex and family history ($p > 0.05$ - **Table 3**). The mean of neuropathy symptom score (NSS) in sub group A was **6.5**, while in sub group B was **6.31 (Table 4)**. There was no statistically significant difference between sub groups A and B as regarding functional status of RA, duration of disease and NSS ($p > 0.05$). There was all patients in sub group A had abnormal findings in clinical examination, while there was only one patient in sub group B had abnormal findings (**Figure 2**). There was a highly statistically significant difference between sub groups A and B as regarding findings of clinical examination ($p < 0.01$).

Table (1): Comparison between control and patient groups in age, sex and family history.

Parameters		Groups	Control group	Patients group	Independent t-test	
			No. = 30	No. = 30	t/X ² *	P-value
Age (years)	Mean ± SD		33.90 ± 8.76	34.10 ± 9.33	0.086	0.932
	Range		22 – 56	21 – 54		
Sex	Female		23 (76.7%)	24 (80.0%)	0.098*	0.754
	Male		7 (23.3%)	6 (20.0%)		
Family history	Negative		22 (73.3%)	19 (63.3%)	0.693*	0.405
	Positive		8 (26.7%)	11 (36.7%)		

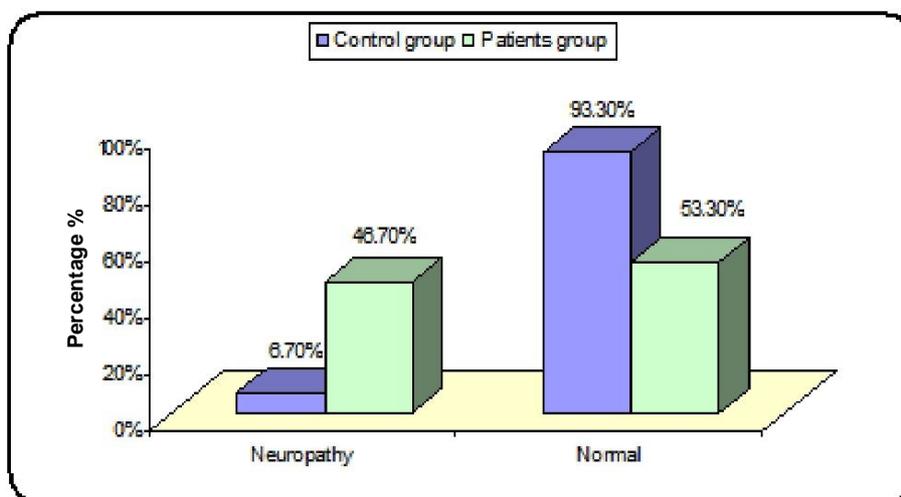


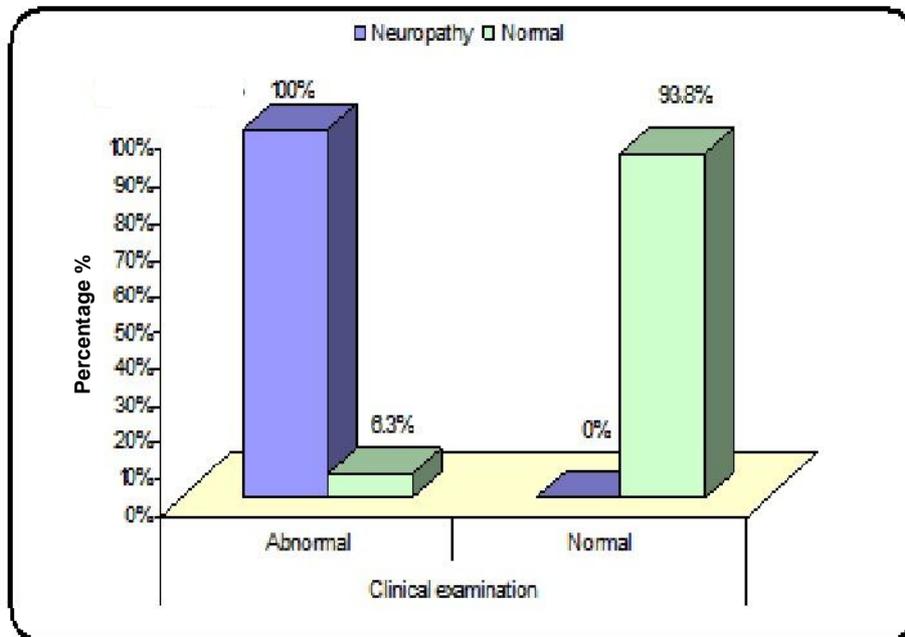
Figure (1): Presence of neuropathy in control and patient groups by NCS and EMG

Table (2): Classification of type and nature of neuropathy in patient group.

Classification		Patients groups	No.	%
Type of neuropathy	Entrapment		8	57.14%
	Mono neuritis simplex		1	7.14%
	Mononeuritis multiplex		2	14.29%
	Polyneuropathy		3	21.43%
Nature of neuropathy	Axonal		4	28.57%
	Demylinating		8	57.14%
	Mixed		2	14.29%

Table (3): Comparison of age, sex and family history between sub groups A (had neuropathy) and B (normal) in patient group,

Patients groups		Neuropathy Sub group A	Normal Sub group B	Independent t-test	
		No. = 14	No. = 16	t/X ² *	P-value
Age	Mean ± SD	38.14 ± 9.01	30.56 ± 8.32	2.395	0.024
	Range	26 – 54	21 – 46		
Sex	Female	10 (71.4%)	14 (87.5%)	1.205*	0.272
	Male	4 (28.6%)	2 (12.5%)		
Family history	Negative	11 (78.6%)	8 (50.0%)	2.625*	0.105
	Positive	3 (21.4%)	8 (50.0%)		

**Figure (2):** Comparison between sub groups A and B as regarding findings in clinical examination.**Table (4):** Comparison in NSS between sub group A and sub group B.

Patients groups		Neuropathy Sub group A	Normal Sub group B	Independent t-test
		No. = 14	No. = 16	P-value
Mean ± SD	6.50 ± 1.22	6.31 ± 1.25	0.682	
Range	5 – 8	4 – 8		

DISCUSSION

In the present study, there was 14 patients had neuropathic affection in electrophysiological study in patient group (46.7%) and this percentage is higher than another study of *Sim et al. (2014)* and to lesser extent lower than another studies *Agarwal et al. (2008)* and *Mohammed et al. (2012)*. In comparison between two sub groups there was the mean of age in sub group A was 38.14 and in sub group B was 30.56, and there was statistically significant difference, there result were in agreement with other studies *Bharadwaj and Haroon (2005)*, *Sherifa et al. (2005)*, *Albani et al. (2006)*, *Agarwal et al. (2008)* and *Sim et al. (2014)*.

There was no relationship between sex and presence of neuropathy in the current study and that in agreement with studies of *Bharadwaj and Haroon (2005)*, *Sherifa et al. (2005)*, *Agarwal et al. (2008)*, *Monodeep et al. (2011)*, *Mohammed et al. (2012)* and *Sim et al. (2014)*. On the other hand, *Albani et al. (2006)* found that male gender to be significantly related to peripheral neuropathy.

In the present study, there was a tightly relationship between abnormal clinical examination and presence of neuropathy, all patients in sub group A had abnormalities in clinical examination such as: muscle weakness, hypo or areflexia in some cases, stock and glove hypothesia, loss of vibration sense, in patients with carpal tunnel syndrome there was positive tinnel sign and positive phalen sign, also on patient with severe carpal tunnel syndrome, there was distal muscle weakness and atrophy in thenar eminence muscle. On the other hand one patient

from sub group B had hyporeflexia in ankle tendon jerk while his electrophysiological study was normal. There results were statistically highly significant and were in agreement to lesser extent to another study of *Agarwal et al., (2008)*.

In sub group A (patients with neuropathy), there were 8 patients had entrapment neuropathy (57.14%), three of them (21.4%) had bilateral Carpal Tunnel Syndrome (CTS), four of them (28.5%) had unilateral CTS, and only one patient (7.14%) had ulnar entrapment neuropathy. These results were similar to other studies *Mohammed et al., (2012)* and *Sim et al. (2014)*. And in contrast with *Agarwal et al. (2008)* and *Monodeep et al. (2011)* due to the variability in selection criteria, duration of disease, and method of diagnosis.

Two patients had mononeuritis multiplex (14.29%) affecting mainly peroneal and ulnar or peroneal and median nerves. Other studies demonstrated mononeuritis multiplex in their studies *Agarwal et al. (2008)*, *Monodeep et al. (2011)* and *Mohammed et al., (2012)*. Three patients had polyneuropathy (21.43%), one of them (7.14%) affecting the nerves of both lower limbs, and two of them (14.28 %) affecting all nerves of upper and lower limbs. These results agreed with studies of *Bharadwaj and Haroon (2005)*, *Mohammed et al. (2012)* and *Sim et al. (2014)*. One patient had mononeuritis simplex (7.14%) affecting superficial peroneal nerve (purely sensory) which agreed with studies of *Bayrak et al. (2010)* and *Mohammed et al. (2012)*.

There was eight patients had demyelinating neuropathy (57.14%), 7 patients of entrapment, and one patient had mononeuritis simplex. Four patients had axonal neuropathy (28.57%), two of them who had mononeuritis multiplex and another two patients had poly neuropathy. Two patients had mixed neuropathy (demyelinating with secondary axonal neuropathy 14.29%) one of them had severe bilateral CTS and the other had poly neuropathy. This result agreed with studies of *Mohammed et al. (2012)* and *Sim et al. (2014)*.

In the current study, the mean of NSS in sub group A (patient with neuropathy) was 6.31 and the mean in sub group B was 6.5 which statistically not significant. This agreed with the study of *Sim et al. (2014)*.

On EMG, the needle muscle study of tibialis anterior, gastrocnemius and quadriceps muscles applied on patients had findings in nerve conduction study only showed on patients with demyelination. No electrical activity was seen at rest, while on volition there was reduction in the number of the motor units recruited. The motor unit action potentials were polyphasic and have increased amplitude with prolonged duration on patients with axonal degeneration. Spontaneous potentials in the form of positive sharp waves, could be present indicating membrane irritability. Fibrillation potentials were also found as well indicating denervation of muscle fibers, which found that there were neurogenic changes in rheumatoid arthritis patients, but no myogenic changes. This result was in agreement with studies of

Mohammed et al. (2012) and Sim et al. (2014).

Finally, our study was limited by its small sample size and cross-sectional design. In addition, we were unable to conduct an electrophysiological study for the same duration from symptom onset. Moreover, we were unable to determine a definite cause of peripheral neuropathy and CTS in this study; whether it was as a result of a direct nerve injury due to joint deformity or it was an independent disease. Further longitudinal studies in a large population are needed.

CONCLUSION

Possibility of presence of peripheral neuropathy in electrophysiological study in patient with rheumatoid arthritis who complain neuropathic symptoms was more than patient who didn't complain. This possibility highly increased in patients who had clinical examination of neuropathy such as hypo or areflexia that we found tightly correlation between clinical examination of peripheral neuropathy and electrophysiological study. The most common type of neuropathy in rheumatoid patients was entrapment neuropathy (as Carpal Tunnel Syndrome). Neurogenic lesions were present, while no myogenic lesion was detected in patients with rheumatoid arthritis.

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دراسة توصيل الأعصاب وتخطيط العضلات في مرضي التهاب المفاصل الروماتويدي

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خلفية البحث : التهاب المفاصل الروماتويدي هو أحد أمراض المناعة الذاتية متعددة الأجهزة؛ وهو يتصف بالتهاب المزمن بالمفاصل الصغيرة والكبيرة؛ مسببا تشوهات مع أعراض مصاحبة خارج المفاصل؛ والتي من أهمها " التهاب الأعصاب الطرفية " .

هدف البحث : هو تقييم العلاقة بين الأعراض المصاحبة لإعتلال الأعصاب الطرفية ونتائج توصيل الأعصاب وتخطيط العضلات في مرضي التهاب المفاصل الروماتويدي.

المرضي وطرق البحث : طبقت هذه الدراسة علي ثلاثين مريضا مصابين بالتهاب المفاصل الروماتويدي من المرضي المترددين علي العيادة الخارجية بقسم الروماتيزم والطب الطبيعي، أو المرضي الذين تم إدخالهم إلي قسم الروماتيزم والطب الطبيعي بمستشفيات جامعة الأزهر. كما طبقت هذه الدراسة علي ثلاثين مريضا آخرين بالتهاب المفاصل الروماتويدي كمجموعة ضابطة ممن لا يعانون من أي دلالة علي إصابتهم بالتهاب الأعصاب سواء بالتاريخ المرضي أو الفحص السريري. وقد تم عمل دراسة توصيل الأعصاب لجميع المرضي في هذه الدراسة متضمنا توصيل العصب الحركي والعصب الحسي بالإضافة إلي موجة اف لكل من العصب المتوسط والزندي والظنبوبي والعصب الشظوي الأصلي، كما تم عمل دراسة تخطيط العضلات للعضلات المصابة فقط .

النتائج : أظهرت الدراسة ما يلي :

- 1- هناك فروق ذات دلالة إحصائية بين مجموعتي المرضي والضابطة فيما يتعلق بوجود دلائل علي التهاب الأعصاب الطرفية في دراسة توصيل الأعصاب.
- 2- هناك فروق ذات دلالة إحصائية بين المجموعتين الفرعيتين المنبثقتين من مجموعة المرضي (مجموعة فرعية أ و ب) فيما يتعلق بسن المرضي في المجموعتين .
- 3- هناك فروق ذات دلالة إحصائية بين المجموعتين الفرعيتين المنبثقتين من مجموعة المرضي (مجموعة فرعية أ و ب) فيما يتعلق بوجود نتائج غير طبيعية في الفحص السريري .

وقد كانت أكثر أنواع الإعتلال العصبي التي وجدت في هذه الدراسة هو إعتلال العصب الإنحساري، وأشهر أنواعه متلازمة النفق الرسغي، يليه إعتلال الأعصاب الكامل، ثم إعتلال العصب الأحادي المتعدد، وأخيرا إعتلال العصب الأحادي البسيط .

الاستنتاج : مرضي التهاب المفاصل الروماتويدي الذين يعانون من أعراض مصاحبة لإعتلال الأعصاب الطرفية أكثر عرضة للإصابة بإعتلال الأعصاب الطرفية من الذين لا يعانون من هذه الأعراض، وأشهر أنواع الإعتلال التي تصيبهم هو إعتلال العصب الإنحساري