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Original Article

Early detection of carpal and tarsal tunnel syndromes in fibromyalgia patients by using electrophysiological and ultrasonographic values

Rheumatology

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ABSTRACT

Background: Carpal tunnel syndrome (CTS) is a focal and compressive neuropathy of the median nerve at the wrist, being the evidence of increasing pressure within the carpal tunnel, Tarsal tunnel syndrome (TTS)is tibial nerve entrapment or neuralgia. The common disorder known as fibromyalgia is characterized by chronic and widespread pain. FM patients also frequently experience headaches, paraesthesia, sleep disturbances, and psychological manifestations. it is important to distinguish between the symptoms of fibromyalgia (FM) and entrapment neuropathies, which are easily misdiagnosed in FM patients, which seems to impact the patient's quality of life when people can't enjoy life because of pain, numbness in the hands, they are exhausted mentally, emotionally, and physically, so we conducted this study for early detection of mild CTS and TTS.

Objective: To assess fibromyalgia as a risk factor in the occurrence of carpal tunnel syndrome and tarsal tunnel syndrome compared to non-fibromyalgia control by using electrophysiological and ultrasonographic values.

Methodology: In this case control study, 100 patients with Fibromyalgia attending the rheumatology and rehabilitation and psychiatric departments of Al Zahraa University Hospital were compared to 100 age-and sex matched apparently healthy people as controls. Tender points count, widespread pain index, symptom severity scale, fibromyalgia score and fibromyalgia impact questionnaire were recorded for FM patients group. The median and posterior tibial nerves were evaluated by electrophysiological studies and by ultrasonography.

Results: The occurrence of tarsal tunnel syndrome and carpal tunnel syndrome is higher in the fibromyalgia group than in the control group in female middle-aged patient, with a statistically significant difference ($p < 0.001$).

Conclusion: Carpal tunnel and tarsal tunnel syndromes were found to be significantly higher in fibromyalgia patients. Musculoskeletal ultrasound is considered as a significant tool for testing for early diagnosis of entrapment neuropathy in cases of FM presented with paresthesia especially when used in combination with electrophysiological.

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Keywords: CTS; TTS; case-control study; fibromyalgia; electrophysiological studies; ultrasound.

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INTRODUCTION

Carpal tunnel syndrome (CTS) is defined as a focal, chronic, and symptomatic compressive neuropathy of the median nerve at the wrist, being the physiological evidence of increasing pressure within the carpal tunnel and the increase of nerve function at the wrist [1]. Tarsal tunnel syndrome (TTS) is a nerve entrapment syndrome causing a painful foot condition in which the tibial nerve is compressed as it travels through the tarsal tunnel , this condition seems to impact the patient's quality of life when people cannot enjoy life because of pain, numbness or weakness in the hands and feet , they are exhausted mentally and emotionally, as well as physically [2].

Common symptoms of fibromyalgia (FM) include chronic, widespread pain and particular tender areas with digital pressure. FM affects between 0.2-6.6% of the world's population, and middle-aged women are impacted more commonly compared to men [3].

Up to 94% of fibromyalgia patients (FMPs) report neurological problems, most likely as a result of a neurological dysfunction, despite the fact that the cause of FM remains elusive. paraesthesia is a frequent condition characterized by sensations of tingling, tickling, pricking, or skin burning that have no obvious physical reason. Prior research has revealed paraesthesia in up to 84% of patients with fibromyalgia [4].

Although the exact mechanism of FM's paraesthesia is unknown, it is thought to arise from the central sensitization Phenomenon, which is an increase in

nociceptive transmission and processing in the central nervous system. Nevertheless, peripheral mechanisms in the nerves and muscles weren't ruled out as potential causes of FM's pain and paraesthesia [5].

The mechanism through which FM produces peripheral nerve entrapment is yet unknown; however, extended periods of immobilization and inappropriate placement of body components are believed to be primary causes of nerve entrapment in FM. Patients with FM experienced significant functional mobility restrictions, specifically challenges with goal-directed movements, as a result of their generalized musculoskeletal pain [6]. The immune profiles of patients diagnosed with CTS with FM are associated with an increase in chemokines and cytokines that modulate systemic inflammation, which can regulate neuropathic symptoms. In addition, a significant relationship was found between CTS severity and serum levels of inflammatory mediators [7].

Entrapment neuropathies of the tibial nerve at the ankle and the median nerve at the wrist cause TTS and CTS, respectively. With a slight female predominance, both conditions predominantly affect adults [8] [9].
It's critical to differentiate FM symptoms in clinical practice from entrapment neuropathies that can be mistakenly diagnosed or overlooked in patients with FM. Consequently, there is a correlation between FM and CTS, which is one of the more prevalent entrapment neuropathies. On the other hand, foot paraesthesia is also uncommon in practice. Thus, to compare the frequency of tibial entrapment neuropathies and median entrapment neuropathies in FM patients, this study was carried out [10].

Numerous neurophysiological techniques, such as sensory and motor nerve conduction studies (NCS), can be employed to evaluate functional alterations in the peripheral nervous system and the activity level of the motor and sensory axons. NCS are a non-invasive, readily measured, safe, and widely accessible method for assessing alterations in the peripheral nervous system [11]. Also, developments in high-resolution ultrasonography have enabled clinicians to investigate peripheral nervous system diseases. The ultrasound shows the extent of abnormalities, which is a complement to the clinical and electrophysiological examination. It is the perfect imaging method for evaluating the peripheral nervous system since it produces high-resolution, radiation-free images, characterizes the movement of tissue in real-time, and shows and analyses the flow of blood using a Doppler [12].

PATIENTS AND METHODS

The current study was conducted on one hundred fibromyalgia patients recruited from Al-Zahraa hospital's rheumatology and rehabilitation department and psychiatric department. The diagnosis of fibromyalgia patients was done as per the 2016 American College of rheumatology criteria. They were 94 females and 6 males; their ages ranged between 21-59 years, with disease duration ranging from 0.5-12 years compared to 100 apparently healthy people of age- and sex matched (82 were females and 18 were males). Their ages ranged between 20-58 years.

Patients younger than 18 years or older than 65 years old and who had a history of connective tissue disorders like rheumatoid arthritis and systemic disorders that affect peripheral nerves, including diabetes mellitus and hypothyroidism, were excluded from the study.

Following an explanation of the procedure, purpose, and importance of the study, each participant has provided written informed consent. The study received approval from the medical ethical committees of Al-Azhar University's, faculty of medicine for girls in Cairo, Egypt (IRB no.1577).

Complete history-taking, general, musculoskeletal, and neurological examinations. The widespread pain index (WPI), symptoms severity scale scores, fibromyalgia impact questionnaire (FIQ), and fibromyalgia severity scores (FS) were assessed and calculated.

Routine laboratory investigations include C-reactive protein (CRP), erythrocyte sedimentation rate, complete blood count, and tests for kidney and liver function.

Motor and sensory NCS of the median, motor medial and lateral planter, and sensory sural nerves, using Neuro EMG Microelectroneuromygraphy (EMG) apparatus from Nihon Kohden Neuropak (Nihon Kohden Corporation, Tokyo, Japan). During the examination, we conducted the nerve conduction protocol at a constant room temperature of 25°C, as advised by Preston and Shapiro (2007) as well as the American Association of Neuromuscular and Electro Diagnostic Medicine (AANEM).

Ultrasonographic evaluation of all study subjects using a 7-11 MHz linear phased array transducer (Xario 200, Toshiba ultrasound machine, Tochigi, Japan).

For the median nerve assessment, the patient was seated with his forearm in a supinated position, resting on a hard, flat surface with his arm extended and his fingers semi-flexed. The median nerve's cross-sectional area (CSA) was measured at the carpal tunnel (between the scaphoid bone laterally and the pisiform bone medially) at the level of the wrist creases. For tibial nerve assessment, the patient in a supine position with a flexed knee and foot on the examination bed. Two specific locations were used for measuring the axial CSA: the distal third of the leg, 10 cm above the beginning of the tarsal tunnel, and inside the tunnel. Measurement was done by tracing a continuous line within the hyper echogenic boundary of the nerves using the measurement tools provided in the US apparatus. Neurophysiologic and ultrasonographic evaluation were carried bilaterally for all study subjects, and the mean of each parameter was considered for comparison so total number 200 hands and feet for each group.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc.,

Chicago, Illinois, USA). Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test**.** The parametric quantitative data were presented as mean± standard deviation and ranges while non-parametric data were presented as median with inter-quartile range (IQR). Also, qualitative variables were presented as numbers and percentages. The following tests were done: Independent-samples t-test of significance was used when comparing between two means ,the comparison between groups with qualitative data was done by using Chi-square test and Fisher's exact test instead of Chi-square test only when the expected count in any cell less than 5 , Pearson's correlation coefficient (r) test was used to assess the degree of association between two sets of variables ,Scatter plot: a graph in which the values of two variables are plotted along two axes, the pattern of the resulting points revealing correlation present ,The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant ≤0.05.

RESULTS

Table 1 shows that there was no statistically significant difference in age or sex between the patients and control groups (p-value >0.05). As regards FM assessment, the mean of Widespread Pain index (WPI) was 14.75±3.40, the mean of Symptom Severity Scale (SSS) was10.03±1.12, while the mean of fibromyalgia Score (FS) was 24.53±3.70. The mean of fibromyalgia impact questionnaire (FIQ) was 76.90±10.29 as shown in table (2).

There were statistically significant different between FM patients and control group regarding sensory median peak latency, sensory amplitude, sensory conduction velocity, motor median latency and the median nerve's CSA as shown in table (3).

Abnormal results detected by NCS of median include: 11 % of FM hands showed prolonged distal sensory peak latency, 6% showed decreased sensory amplitude and 7% showed decreased sensory conduction velocity. And 5% of FM hands showed prolonged motor median latency.
While by US examination of CSA of median nerve, 77.5 % FM hands showed increased CSA as shown in table (3).

It was found that there were significant differences between the two groups in the values of amplitude, lateral planter latency, medial planter latency, tibial nerve's CSA at the tunnel, 10 cm above the tunnel, and difference between CSA at the two levels of measurement as shown in table (4).

Abnormal NCS results of posterior tibial nerve, we found that 3 % and 21% of FM feet showed prolonged motor latencies of medial planter nerve and lateral planter nerve respectively.

While by US examination of CSA of tibial nerve, 50% of FM patients showed increased CSA of the tibial nerve at tunnel, 33 % of them showed an increased CSA at 10 cm above the tunnel and 31% showed increased CSA difference of the tibial nerve between two levels as shown in table (4).

There was a statistically significant positive association between disease duration (years) with lateral planter nerve latency which mean increased frequency of TTS and the ultrasonographic CSA of the median nerve which mean increased frequency of CTS, with p-values (p<0.05) as displayed in figures (1) and (2).

Regarding disease related parameters which assess disease severity, there was significant positive correlation between median sensory latency with FIQ. Also there was significant positive correlation between WPI and CSA of tibial nerve at tunnel as displayed in figures (3) and (4).

Table (1): Comparing demographic data of the patients with controls

Demographic data	Patients Group n = 100	Control Group n = 100	Statistical test	p-value
Age (years) - Mean ±SD (years) - Range (years)	 35.28±9.21 21-59	 34.76±8.45 20-58	**t –test** 1.682	0.376
Sex - Female - Male	94 (94.0%) 6 (6.0%)	82 (82.0%) 18 (18.0%)	**x^2=2.818**	0.331
Disease duration (years) - Range (years)	0.5-12	---	---	---

t-test: Independent t-sample t-test, x^2: Chi-square test, *: Significant p-value (<0.05)

Table (2): Patient data according to disease-related parameters

Disease related parameters	FM group n = 100
WPI	
- Mean ±SD	14.75±3.40
- Range	6-19
SSS	
- Mean ±SD	10.03±1.12
- Range	8-12
FS	
- Mean ±SD	24.53±3.70
- Range	16-31
FIQ	
- Mean ±SD	76.90±10.29
- Range	51-93

WPI: Widespread pain index, SSS: Symptom severity scale, FS: Fibromyalgia score FIQ: Fibromyalgia impact questionnaire

Table (3): Comparison of the study parameters for the motor and sensory median nerve conduction and CSA of median nerve for both hands of the patient group and the control group

Parameters	Patients Group n = 100 Mean ± SD	Control Group n = 100 Mean ± SD	t-test	p-value	Affection (CTS)
Median motor latency (ms)	3.18±0.73	2.98±0.65	2.046	0.042*	**5%**
Median motor amplitude (mv)	9.82±2.28	10.08±2.40	0.785	0.433	**1%**
Median motor conduction velocity (m/s)	56.53±6.62	58.22±6.10	1.877	0.062	**0%**
Median sensory Latency (ms)	2.88±0.55	2.72±0.48	2.192	0.030*	**11%**
Median sensory amplitude (µv)	19.40±5.99	23.48±5.37	-7.172	0.001*	**6%**
Median sensory conduction velocity (m/s)	56.23±4.62	58.10±4.38	4.153	0.001*	**7%**
Median nerve CSA at carpal tunnel (mm^2)	13.38±2.56	10.04±1.08	17.037	0.001*	**77.5%**

CSA: Cross-sectional area, t-test: Independent t-sample t-test; *: Significant p-value (<0.05)

Table (4): Comparison of posterior tibial nerve motor nerve conduction and CSA of tibial nerve for both feet in patient and control groups

Parameters	Patient Group n = 100 Mean ± SD	Control Group n = 100 Mean ± SD	t-value	p-value	Affection (TTS)
Medial planter latency (ms)	4.46±0.74	4.26±0.68	1.990	0.048*	**3 %**
Medial planter amplitude (mv)	10.93±3.06	11.92±2.98	0.785	0.433	**2%**
Medial planter conduction velocity (m/s)	48.97±6.41	50.06±5.61	1.810	0.071	**1.5%**
Lateral planter latency (ms)	5.94±1.05	5.64±0.61	2.470	0.014*	**21%**
Lateral planter amplitude (mv)	5.40±1.73	6.52±1.14	-7.658	0.001*	**12%**
Tibial nerve CSA at tarsal tunnel (mm2)	13.25±4.06	10.62±0.85	8.961	0.001*	**50%**
Tibial nerve 10 cm CSA above tarsal tunnel (mm^2)	11.28±2.15	10.15±0.96	6.827	0.001*	**33%**
CSA difference between two levels (mm^2)	2.05±2.46	0.48±0.51	8.825	0.001*	**31%**

CSA: Cross sectional area, t-test: t-Independent sample t-test; *: Significant p-value (<0.05).

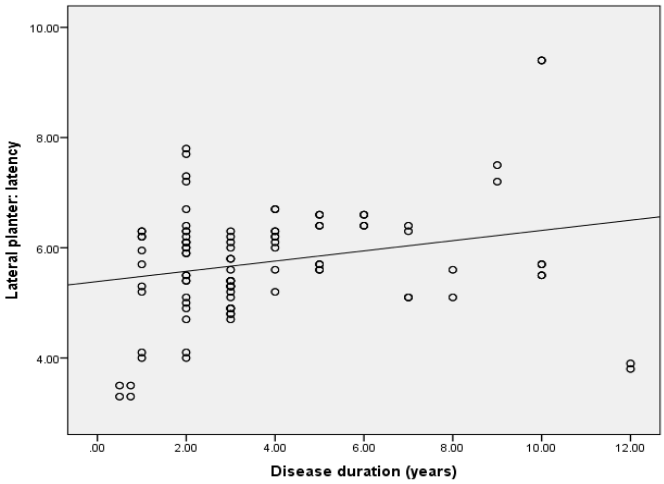

Figure (1): Scatter plot between disease duration "years" with lateral planter nerve latency among cases

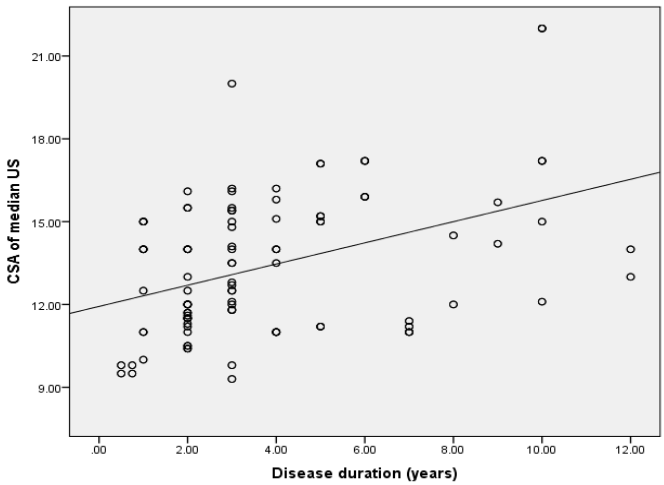

Figure (2): Scatter plot between disease duration "years" with CSA of median nerve among cases

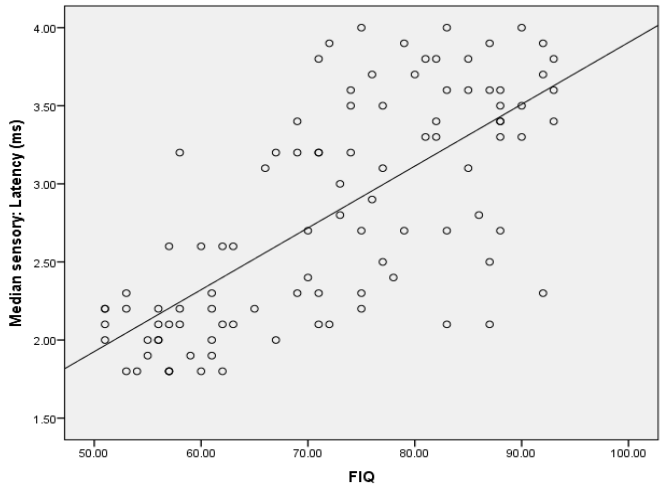

Figure (3): Scatter plot between fibromyalgia impact questionnaire (FIQ) with Median sensory: Latency "ms" among cases

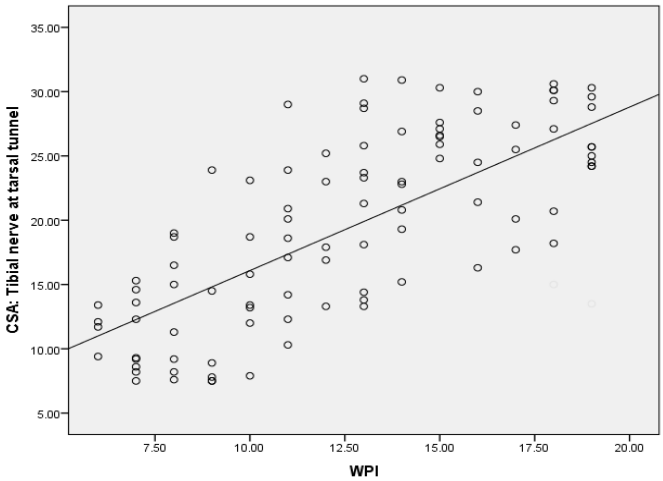

Figure (4): Scatter plot between WPI with CSA: Tibial nerve at tarsal tunnel among cases

DISCUSSION

The present work studied that fibromyalgia playing a role in frequency of CTS and TTS with and the accuracy of ultrasonography for diagnosing CTS and TTS in comparison with conventional neuro-physiological testing.

In the current study, there was an increased frequency of median sensory nerve abnormalities compared with median motor nerve abnormalities in FM patients. This result agrees with Werner et al. [13], as they reported that the abnormalities of the median sensory fibers precede motor fiber affection in documenting CTS. They attributed this to sensory fibers having a greater percentage of big, myelinated fibers that have greater energy consumption and are therefore more susceptible to ischemia injury. In another study on 102 FM patients [14] investigated the connection between the activity of the disease and quality of life in fibromyalgia patients who have CTS. They found that, there was significantly prolonged mean distal motor latency of median nerve in FM patients when compared with the control group which agree with the results of this study.

In the current study, ultrasonographic scanning of the median at the tunnel was carried out in FM patients and revealed significantly increased mean CSA at the tunnel in comparison with the control group. These results are supported by Kudo et al. [15] who studied the ultrasonography's diagnostic value in comparison to nerve conduction studies in individuals with unilateral CTS and found that diseased hands with CTS had significantly increased mean median nerve CSA at the tunnel. These results were disagreed with by Silva et al. [16], who studied CTS by ultrasonography in 41 FM patients and 42 healthy control subjects and reported that there was no significant statistical difference among the groups and concluded that it would be difficult to clinically distinguish FM patients with CTS from those without it, but these results had some limitations as they had a small sample size compared with the current study. However, our findings were in disagreement with those of El-Hewala et al. [17], who observed that electrophysiological investigations were able to identify a greater number of posterior TTS cases when comparing electrophysiological and US diagnoses of the condition. While MSUS can only identify the syndrome in 8 (16%) cases, electro-physiology was able to identify the syndrome in 18 (36%) cases.

When compared to control subjects' extremities, FM patients' extremities in this study had a significantly greater incidence of focal entrapment neuropathy. Leblebicier et al. [18] studied the prevalence of tarsal tunnel syndrome (TTS) in patients with fibromyalgia (FM) and reported that, when compared to control individuals, the incidence of focal entrapment neuropathy in the extremities of patients with FM was significantly greater. These results were linked to weight gain, lengthy periods of immobilization, and inappropriate positions of parts of the body as a result of widespread musculoskeletal pain, all of which are biomechanical variables consequent to hypermobility. Jackson et al. [19] hypothesized that electrodiagnostic measures are abnormal only when large, myelinated fibers have significant demyelination or axonal loss. Despite this, an extremely significant positive connection between electrodiagnostic measures and ultrasonography was discovered. This hypothesis may explain the increased incidence of abnormally large CSA of the median nerve detected by ultrasonography compared with the less abnormal electrophysiologic results in FM patients in the current study.

It is worth mentioning that, although nerve conduction studies are the standard diagnostic and most accurate tests for studying peripheral nerve entrapment, high-frequency ultrasonography gives an opportunity to detect abnormally increased CSA median and tibial nerves, which may occur early and precede nerve conduction study abnormalities in the syndromes of tarsal tunnel and carpal tunnel.

CONCLUSION

Both the syndromes of tarsal tunnel and carpal tunnel are significantly increased in fibromyalgia patients when compared with non-fibromyalgia control subjects. CTS

and TTS correlate with disease severity in fibromyalgia. Fibromyalgia patients presented with symptoms of carpal tunnel or tarsal tunnel syndrome could be evaluated with electrophysiological studies as well as ultrasonography for early diagnosis of entrapment neuropathy.

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Conflict of interest: No conflict of interest

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الملخص العربي

الكشف المبكر عن متلازمات النفق الرسغي ونفق عظم الكعب لدى مرضى الفيبروميالجيا باستخدام القيم الفيزيولوجية الكهربية والموجات فوق الصوتية

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ملخص البحث

الخلفية: متلازمة النفق الرسغي هي اعتلال عصبي بؤري وانضغاطي للعصب المتوسط في الرسغ، وهي دليل على زيادة الضغط داخل النفق الرسغي، ومتلازمة نفق عظم الكعب هي انحباس العصب الظنبوبي أو الألم العصبي. يتميز الاضطراب الشائع المعروف باسم الفايبروماليجيا بألم مزمن وواسع الانتشار. يعانى مرض الفايبروماليجيا أيضًا في كثير من الأحيان من الصداع والخدر واضطرابات النوم والاعراض النفسية. من المهم التمييز بين اعراض الفايبروماليجيا والاعتلال العصبى الانحباسى , و التى يتم تشخيصها بشكل خاطئ بسهولة لدى مرضى الفايبروماليجيا والتي بدورها قد تؤثر على نوعية حياة المريض عقليًا وعاطفيًا وجسديًا عندما لا يستطيع الاستمتاع بالحياة بسبب الألم، والخدر في اليدين، والإرهاق. ، لذلك أجرينا هذه الدراسات للكشف المبكر عن حالات متلازمات النفق الرسغى ونفق عظم الكعب.

الهدف: هو تقييم الفيبروميالجيا كعامل خطر في حدوث متلازمة النفق الرسغي ومتلازمة النفق عظم الكعب مقارنة بالأشخاص الطبيعية باستخدام القيم الفيزيولوجية الكهربائيه والموجات فوق الصوتية.

الطرق: هذه دراسة الحالات والشواهد ، تمت مقارنة 100 مريض مصاب بالفيبروميالجيا ويترددون على أقسام الروماتيزم وإعادة التأهيل والطب النفسي في مستشفى الزهراء جامعة الأزهر مع 100 من الأشخاص الأصحاء ظاهريًا من حيث العمر والجنس. تم تسجيل عدد نقاط العطاء، ومؤشر الألم على نطاق واسع، ومقياس شدة الأعراض، ودرجة الفيبروميالجيا واستبيان تأثير الفيبروميالجيا لمرضى الفايبروميالجيا. تم تقييم الأعصاب الظنبوبية المتوسطة والخلفية من خلال الدراسات الفيزيولوجية الكهربائيه والتصوير بالموجات فوق الصوتية.

النتائج :تبين أن حدوث متلازمة النفق الرسغي ومتلازمة النفق الرسغي أعلى في مجموعة الألم العضلي الليفي منه في المجموعة الضابطة لدى المريضات في منتصف العمر، مع وجود فرق ذو دلالة إحصائية.

الاستنتاجات: تم العثور على زيادة كبيرة في متلازمة النفق الرسغي ومتلازمة النفق عظم الكعب لدى مرضى الفيبروميالجيا. تعتبر الموجات فوق الصوتية العضلية الهيكلية أداة مهمة لاختبار التشخيص المبكر للاعتلال العصبي الانحباسي في حالات الألم العضلي الليفي المصحوبة بتنميل وخاصة عند استخدامها مع الفيزيولوجية الكهربائيه.

الكلمات المفتاحية: متلازمة نفق الرسغي، متلازمة عظم الكعب ، دراسة الحالات والشواهد، الفايبروميالجيا، الدراسات الفيزيولوجية الكهربائيه، السونار.

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