JEIMP
E-ISSN: 2980-0617

The Journal of
European Internal Medicine Professionals

JEIMP
The Science

Original Article

Neuromuscular Dysfunction and Electrophysiological Findings in Patients With Hypothyroidism and Hyperthyroidism

Author(s) [1]Arzu Akgül, [2]Lale Akbulut Aktekin, [3]Erdal Eskioğlu

Affiliation(s)
[1]Etlik City Hospital, Department of Nephrology, Ankara, Turkey
[2]Private Clinic, Ankara, Turkey
[3]Mamak Su Medical Center, Ankara, Turkey

Corresponding Author Arzu Akgül, Etlik City Hospital, Department of Nephrology, Ankara, Turkey.
E-mail: arzuakgul@gmail.com

10.5281/zenodo.10635564

J Eur Int Prof. Year; 2024, Volume: 2, Issue: 1 *Submitted at*: 05.09.2023, *Accepted at*: 04.10.2023, *Published at*: 15.02.2024

JEIMP belongs to "*The Foundation for the Management of Chronic Diseases***" and is supervised by the MKD Digital Publishing.** *www.jeimp.com and digitalmkd.com*

Abstract

Background: We aimed to determine the frequency of neuropathy and myopathy in newly diagnosed hypothyroid and hyperthyroid patients and to investigate the correlation between serum creatine kinase (CK) concentration and thyroid dysfunction.

Methods: A total of 21 hyperthyroid, 19 hypothyroid, and 20 healthy control subjects were selected for the study. All participants underwent neuromuscular examinations for paresthesia, diffuse pain, muscle cramps, and muscle weakness. Electroneurophysiologic studies were performed on all participants.

Results: Neuromuscular complaints were observed more frequently in the hypothyroid and hyperthyroid groups compared to the control group. Myopathy was detected in 10% of the hypothyroid group and 4% of the hyperthyroid group. Polyphasia potential abnormality was detected in 21% of the hypothyroid group and 14% of the hyperthyroid group. CK elevation was found in 42% of patients in the hypothyroid group and 4% of patients in the hyperthyroid group. There was no correlation between symptoms and CK elevation or between myopathy and thyroid function levels. In the electroneurophysiologic study, 14% neuropathy was found in the hyperthyroidism group and 26% in the hypothyroidism group. In the hypothyroid group, polyneuropathy was found in 10%, and carpal tunnel syndrome was found in 10%. Absence of sensory action potential was found in 10% of the hyperthyroid group and 4% of the hypothyroid group, and low compound muscle action potential was found in 4% of the hyperthyroid group. There was no correlation between thyroid hormone levels and neuropathy.

Conclusion: Neuromuscular complaints and neuropathic findings are highly prevalent in patients with thyroid dysfunction. Neuromuscular symptoms may improve after treatment of thyroid disease. In future studies, comparing post-treatment electrophysiologic values with pre-treatment values and clinical values may more clearly demonstrate the effect of thyroid function on the neuromuscular system.

Keywords: Hypothyroidism, hyperthyroidism, neuromuscular

INTRODUCTION

Thyroid dysfunctions are significant endocrine disorders common among adults and may be associated with morbidity and mortality, especially in elderly individuals. Both hypothyroidism and hyperthyroidism can cause signs and symptoms of neuromuscular dysfunction (1,2). In hypothyroidism, myopathy characterized by proximal muscle weakness may be observed alongside mononeuropathy and sensorimotor axonal polyneuropathy. The prevalence of these symptoms and findings varies in different publications. In previous studies, the prevalence of neuropathy in hypothyroid patients ranged from 10% to 70%, while the prevalence of myopathy ranged from 20% to 80%. Electrophysiologic studies have shown that carpal tunnel syndrome (CTS) is the most common neuropathy in hypothyroidism (3-5).

In hyperthyroidism, myopathy, mononeuropathy, and sensorimotor axonal polyneuropathy may be observed with a less prevalence Neuropathy is less frequent

and typically subclinical in hyperthyroidism. It is believed that weight loss, weakness, infiltration of the tendon sheath with mucopolysaccharides, infiltrative dermopathy, and the direct effects of thyroid hormones on axonal function may contribute to the development of mononeuropathy in thyrotoxic patients. In hyperthyroid patients, the prevalence of myopathy ranged from 60% to 80%, while polyneuropathy and neuropathy were rarely reported, with low prevalence in a few publications (6-9).

The aim of our study was to investigate the prevalence of neuromuscular symptoms in newly diagnosed hypothyroid and hyperthyroid patients, to demonstrate neuromuscular dysfunction using electroneurophysiology, and to determine the possible correlation with creatine kinase (CK) concentration and serum thyroid hormone levels in the presence of neuropathy and myopathy.

METHODS

Twenty-one patients with hyperthyroidism (14 females/7 males) and 19 patients with hypothyroidism (17 females/2 males), who had not received a previous hormone replacement therapy, and whose symptoms had lasted for more than one month, were included in the study. Twenty healthy volunteers with no previous history of thyroid disease and who were clinically and biochemically euthyroid were assigned as the control group.

Patients over 65 and under 18 years of age, with chronic diseases (such as diabetes mellitus, malignancy, chronic liver disease, chronic renal failure, collagen tissue diseases), vitamin B12 and folic acid deficiency, chronic alcohol use, a history of drug use causing neuropathy and myopathy, and central or peripheral nervous system diseases were excluded.

Symptoms of the participants; such as paresthesia, muscle cramps, muscle weakness, and diffuse pain fatigue were noted. Subjective symptoms were thoroughly evaluated by performing physical examination. Serum creatinine kinase (CK) levels, nerve conduction studies, and needle electromyography (EMGs) were assessed retrospectively from hospital files.

Electroneurophysiologic studies were conducted using the Nihon Kohden Neuropack 2 device in all patients and the control group in accordance with the American Diabetes Association diabetic neuropathy protocol. Median motor conduction studies, ulnar, peroneal, and motor nerve conduction velocities, distal latencies, and compound muscle action potentials (CMAPs) were examined. In sensory conduction studies, median, ulnar, and sural nerve sensory conduction velocities, distal latencies, and sensory amplitude potentials (SAP) were measured. Deviations from reference values were recorded according to recommended protocols. The presence or absence of polyneuropathy (PNP) was determined by electrophysiologic involvement of more than one of the examined nerves, with pathologic findings of the involved nerves (SAP decrease, decrease in sensory conduction velocity, slowing, prolongation in motor nerve distal latency, CMAPS decrease in amplitude, slowing of motor conduction velocity, F-wave latency prolongation) evaluated based on the fulfillment of at least one of these criteria.

The presence of spontaneous muscle fibril activity (fibrillation potentials, positive sharp waves, fasciculations, or complex repetitive discharges) and signs of reinnervation activity (polyphasic or giant motor unit action potential) were measured. A visual analysis method was used to measure motor unit action potential (MUAP) values.

This study was conducted in agreement with the Declaration of Helsinki-Ethical principle for medical research involving human subjects.

STATISTICAL ANALYSIS

SPSS version 10.0 for Windows was used in the assessment of the study data. The distributions of numeric variables were assessed using both the Kolmogorov-Smirnov test and the Shapiro-Wilk test. Parametric variables were presents as mean ± standard deviation. Anova and posthoc Tukey tests were used in the comparison of multiple groups. Categorical variables were exhibited by number and percentage. Spearman correlation coefficient was applied for the analyses of nonparametric data. Pearson's chi-square test was used to compare categorical variables. The level of statistical significance was set at $P<0.05$.

RESULTS

A total of 40 patients (31 females and 9 males) with a diagnosis of hypo or hyperthyroidism were evaluated. The mean ages were 42.23±12.09 and 40.47±14.11 years in hypothyroidism and hyperthyroidism groups, respectively. The control group consisted of 20 healthy individuals with a mean age of 42.25±12.01 years (**Table 1**).

Table 1. Clinical and laboratory characteristics of hypothyroidism and hyperthyroidism patients

	Hypothyroidism (n=19)	Hyperthyroidism (n=21)	Control group (n=20)	P[1]	P[2]
Age (year)	40.47±14.11	42.23±12.09	40,38±9,27	0.870	0.571
sT3(pg/ml)	1.38±0.39	12.62±5.78	2.73±0.40	0.001*	0.001*
sT4 (ng/dl)	0.62±0.82	4.04±1.94	1.12±0.20	0.001*	0.001*
TSH (mIU/ml)	74.21±33.9	0.059±0.002	1.89±0.87	0.001*	0.001*
CK (IU/l)	336.21±140	80.52±64.88	83.12±37.46	0.001*	0.752

*: p<0.05, TSH: Tiroid Stimulan Hormon, fT4: free T4, fT3:serbest T3, CK: Creatinin Kinase. n: Patient number P1: Significance value between hypothyroidism and control group, P2: Significance value between hyperthyroidism and control group

Table 2. The neurological complaints of the patient and control groups

	Hypothyroidism (n:19)	Hyperthyroidism (n:21)	Control (n:20)	P[1]	P[2]
Weakness	15 (78.9 %)	17 (80.9 %)	6 (30%)	0.004	0.002
Cramps	16 (84.2%)	11 (52.3%)	2 (10%)	<0.001	0.006
Paresthesia	15 (78.9%)	10 (47.6%)	2 (10%)	<0.001	0.015
Diffuse pain	13 (68.4%)	14 (66.6%)	3 (15%)	0.001	0.001

n: Patient number P1: Significance value between hypothyroidism and control group, P2: Significance value between hyperthyroidism and control group

Clinical and laboratory features of the participants were given in **Table 1**. The neurological symptoms of patients including weaknes, cramping, paresthesia, diffuse pain were more common in hypothyroidism and hyperthyroidism groups compared the control group ($p<0.05$) (**Table 2**). The prevalence of symptoms in patients with abnormal thyroid hormone status as follows; weakness 80.9% (in hyperthyroidism) and 78.9% (in hypothyroidism), cramping 52.3% (in hyperthyroidism) and 84.2% (in hypothyroidism), paresthesia 47.6% (in hyperthyroidism) and 78.9% (in hypothyroidism), and diffuse pain 66.6% (in hyperthyroidism) and 68.4% (in hypothyroidism). The prevalence of neuromuscular complaints in the control group was lower than in the hypothyroid and hyperthyroid patient groups ($p<0.05$). Neurological examinations suggesting myopathy or polyneuropathy (PNP) did not reveal weakness, decreased deep tendon reflexes, or glove-sock-style sensory deficits.

Electrophysiologic studies revealed myopathy in 2 patients (10%) and polyphasia potential abnormalities in 4 patients (21%) in the hypothyroid group. In the hyperthyroidism group, myopathy was detected in 1 patient (4%) and polyphasia potential abnormalities in 3 patients (14%).

Since myopathy was detected in only 1 patient in the hyperthyroidism group, the relationship between CK and thyroid functions was not evaluated. In the hyperthyroidism group, serum CK concentration was elevated in 1 patient (4%). In hypothyroid patients, CK concentration was elevated in 8 patients (42%), and there was no significant correlation between serum T3 and T4 levels and myopathy ($p>0.05$).

There was no statistically significant correlation between neuromuscular symptoms and CK concentration in both groups ($p>0.05$). There was no significant difference in CK concentration between patients with electroneurophysiologically detected myopathy and patients without myopathy ($p>0.05$). There was no significant difference in sT3, sT4, and TSH values between patients with high CK concentrations and patients with normal levels ($p>0.05$).

The findings of the hypothyroidism and hyperthyroidism groups and the control group in the electroneurophysiologic studies are presented in **Table 3**. Median nerve motor and sensory amplitudes, as well as ulnar nerve sensory amplitude, were lower in hyperthyroid patients compared to the control group ($p<0.05$). Median nerve motor and sensory amplitudes were also lower in hypothyroid patients compared to the control group ($p<0.05$) (**Table 4**).

In the hypothyroidism and hyperthyroidism groups, decreased sural nerve sensory conduction velocity and absence of SAP were detected, although not statistically significant, sural nerve sensory conduction velocity was found to be lower than in the control group. This suggests that sensorial conduction may be impaired earlier than motor conduction in thyroid dysfunctions.

There was no statistically significant difference between the serum sT3 and sT4 levels of patients with neuropathy and thyroid patients without neuropathy ($p>0.05$). No electrophysiologic neuropathy was detected in the control group. The incidence of neuropathy was higher in patients with thyroid dysfunction compared to the control group, and this difference was statistically significant ($p<0.05$).

DISCUSSION

This study demonstrates that symptoms such as weakness, cramps, paresthesia, and pain are more common in patients with hypothyroidism and hyperthyroidism, and these patients may exhibit electroneurophysiological findings more frequently than individuals with normal

Table 3. Electroneurophysiologic Neuropathy Findings in Hypothyroidism-Hyperthyroidism and Control Group

	Hyperthyroidism (n:21)	Hypothyroidism (n:19)	Control (n:20)
Normal	18	14	20
Polyneuropathy	0	2	0
Sural conduction velocity decrease or no SAP	2	1	0
CTS	0	2	0
Peroneal CMAP amplitüd low	1	0	0

SAP: Sensory amplitude potential CTS:carpal tunnel syndrome CMAPS: compound muscle action potentials

Table 4. Comparison of the groups according to the electroneurophsiological findings

		Hyperthyroidism Group	Hypothyroidism Group	Control Group	Normal Value	P[1]	P[2]
	D lat	3.04± 0.08	3.10± 0.08	3.15± 0.05	<3.6 m/sn	0.2	0.51
Median	Amp	9.07± 0.97	9.19± 0.93	11.84± 0.95	> 5 mV	0.027*	0.034*
Motor	NCV	58.39± 0.83	56.54± 1.26	57.35± 0.82	> 49.96 m/sn	0.382	0.643
	F	27.66± 0.42	27.71± 0.55	26.99± 0.3	<29.7 m/sn	0.192	0.683
Median	NCV	46.07± 0.68	45.93± 1.27	46.97± 0.92	>41.26 m/sn	0.715	0.615
	Amp	25.54± 2.45	25.49± 2.5	31.22± 3.33	> 10 mV	0.044*	0.042*
	D lat	2.30± 0.04	2.40± 0.1	2.29± 0.03	<2.51 m/sn	0.824	0.97
Ulnar	Amp	10.22± 0.59	12.26± 0.7	13.06± 0.51	> 5 mV	0.002*	0.177
Motor	NCV	61.32± 1.41	58.04± 1.08	61.26± 1.22	> 50.61 m/sn	0.917	0.126
	F	27.35± 0.48	27.17± 0.38	27.20± 0.27	<30.26 m/sn	0.927	0.694
Ulnar	Amp	19.07± 1.27	21.02± 1.87	18.02± 0.87	> 8 mikroV	0.392	0.112
	NCV	43.32± 0.75	45.30± 0.87	44,57± 0,46	> 39.26 m/sn	0.667	0.627
	D lat	3.72± 0.11	4.39± 0.22	3.80± 0.15	<4.78 m/sn	0.705	0.039
Peroneal	Amp	6.05± 0.69	6.54± 0.74	8.04± 0.77	> 4 mV	0.087	0.423
Motor	NCV	47.19± 0.72	46.87± 0.77	48.24± 0.80	>41.83 m/sn	0.279	0.152
	F	45.88± 0.69	48.38± 0.9	46.62± 0.72	<55.38 m/sn	0.389	0.292
Sural	NCV	38.9	38.4	39.38± 0.72	> 34.68 m/sn	0.483	0.383
	Amp	15	20.8	27.65± 3.56	> 6 mikroV	0.327	0.173

D lat: Distal latency, Amp: Amplitude, NCV: Nerve conduction velocity, F: F latency, p1: Significance value between hyperthyroidism and control group, p2: Significance value between hypothyroidism and control group. *:P<0.05

thyroid hormone levels.

The prevalence of neuromuscular involvement in thyroid dysfunction varies between 20% and 80% (3,10-13). Approximately 40% of hypothyroid patients and 20% of hyperthyroid patients show predominantly sensory signs of sensorimotor axonal neuropathy early in the course of thyroid disease (3). In our study, the frequency of cramps increased in both patient groups, and fatigue complaints were reported by 80% of the patients, while the frequency of diffuse pain and paresthesia increased.

Although neuropathies seen clinically and electrophysiologically in hypothyroidism and hyperthyroidism are often sensorial, mixed sensorial and sensorimotor neuropathies may be present in the early stages of the disease. Motor nerve conduction velocity is generally within normal limits, but sensorial nerve action potentials may be decreased in the early stages of the disease (14).

Hypothyroidism affects many systems, including the central and peripheral nervous system. Some publications suggest that electroneurophysiological abnormalities, such as decreased motor and sensorial nerve conduction velocity, may be observed (15-16). Electrophysiological studies of peripheral neuropathy in hypothyroid patients yield findings varying between 17% and 72% (3,17,18). The development of peripheral neuropathy in hypothyroidism may be due to various causes, such as the accumulation of mucopolysaccharides in the endoneurium and perineurium, segmental demyelination, glycogen aggregates, and axonal degeneration (19). In a study by Khedr et al., an electroneurophysiological study was conducted in 23 patients with hypothyroidism, and it was found that the peripheral nervous system was affected in 52% of the patients, with entrapment neuropathy developing in 35% of them, myopathic changes in 9%, and axonal polyneuropathy in 9% (15). While neuropathy due to hypothyroidism has been demonstrated in studies, neuropathy due to hyperthyroidism is reported to be less common. Duyff et al. found a neuropathy rate of 19% in patients with hyperthyroidism in their study (3). In a study by Berlit et al., 27 hyperthyroid patients were examined neurophysiologically (20). Although motor nerve conduction velocities of the peroneal and median nerves were mostly normal in patients, 29.6% exhibited pathologic findings in the sensorial nerve conduction velocities of the sural nerve, and 22.2% had borderline findings.

In our study, among patients with thyroid dysfunction, the rate of neuromuscular complaints was higher than in the control group. Neuropathy rates were 26% in the hypothyroid patient group and 14% in the hyperthyroid patient group. Polyneuropathy was found in 10% of the hypothyroid patient group but not in the hyperthyroid patient group. However, the absence of sensory action potentials or decreased sural nerve conduction velocity was found in 9%, and low compound muscle action potential was found in 4% in the hyperthyroid patient

group. The reasons for the varying frequency of peripheral neuropathy in studies may be attributed to differences in the criteria used to diagnose peripheral neuropathy in the literature. Median nerve motor and sensorial amplitudes, as well as ulnar nerve sensorial amplitude, were lower in hyperthyroid patients compared to the control group. In hypothyroid patients, median nerve motor and sensory amplitudes were also lower than in the control group, with the decrease in sensory amplitude being more pronounced. The rate of sural sensory conduction velocity decrease was high in both patient groups. This suggests that sensory conduction is impaired earlier than motor conduction in thyroid dysfunctions. Akarsu et al. found that axonal motor fibers were mostly affected in hypothyroidism, while Duffy et al. emphasized that the sensory conduction system was affected earlier than the motor conduction system in thyroid dysfunctions based on electrophysiological findings (3,13).

Carpal tunnel syndrome is one of the most common entrapment neuropathies. In hypothyroidism, CTS is thought to develop due to mucinous infiltration of the median nerve perineurium and endoneurium. The association of hypothyroidism and CTS has been reported with varying rates in the literature. Suresh et al. reported that thyroid dysfunction (hypothyroidism or hyperthyroidism) slightly increased the rate of CTS in their study (21). Van Dijk et al. found a prevalence of hypothyroidism between 1.3% and 10.3% in patients with CTS in their review (22). While the rate of CTS in patients with subclinical hypothyroidism was found to be 12.5%, CTS was detected at a higher rate of 32.5-37.5% in patients with overt hypothyroidism (22-24). Apart from differences in diagnostic criteria, other factors, such as gender, advanced age, and duration of hypothyroidism, may influence the prevalence of CTS in hypothyroid patients (23).

There are few studies investigating the prevalence of CTS in patients with hyperthyroidism. Çakır et al. found a 7.1% prevalence of CTS with nerve conduction tests in patients with thyrotoxicosis (42 patients) (8). In their study, CTS was not detected in any of the 23 patients with subclinical thyrotoxicosis. In our study, the incidence of carpal tunnel syndrome was found to be 10% (2/19 patients) in the hypothyroid patient group, supporting the literature, while no carpal tunnel syndrome was observed in the hyperthyroid patient group.

Myopathy is a well-recognized complication of hypothyroidism. Khaleeli et al. found myopathy in 80% of 15 patients with severe hypothyroidism and suggested that myopathy was more frequent in patients with serous effusion and may be related to the degree of hypothyroidism (24). They found no statistical significance between myopathy and disease duration. Khedr et al. examined 23 hypothyroid patients electrophysiologically and found myopathy in 2 patients (9%), while Duyff et al. found a myopathy rate of 33% (3,15). Although the severity of myopathy is often correlated with the degree and duration of hypothyroidism in electrophysiological examinations, there is no consistent correlation between myopathy findings in muscle tissue obtained via needle biopsies and the duration and severity of hypothyroidism (11). EMG findings in hypothyroidism are quite variable, and EMG is often observed as normal. Rarely, typical myopathic patterns and abnormal spontaneous activities may be observed on EMG (24). These rate variations may be attributed to this variability.

The incidence of muscle dysfunction in hyperthyroidism can be up to 80%. However, although this rate seems to reflect the frequency of myopathy, it cannot be supported by electrophysiological studies. The mechanism of myopathy in hyperthyroidism is thought to be related to the decrease in muscle function due to the increased myosin alpha concentration in skeletal muscle with adrenergic stimulation of thyroid hormones (6). Duyff et al. found myopathic changes in 10% of 21 hyperthyroid patients electrophysiologically and reported a correlation between muscle weakness clinically and elevated T4 levels (3).

In our study, myopathy was found in 2 patients (10%), and electrophysiologically increased polyphasia was observed in 4 patients (20%) in the hypothyroid group. These findings were not correlated with TSH, sT3, sT4 values. In the hyperthyroid patient group, myopathy was detected in 1 patient (4%), and electrophysiologically increased polyphasia was observed in 3 patients (14%).

Serum CK concentration is usually elevated in hypothyroid patients. Rarely, hypothyroidism may cause severe skeletal muscle involvement and rhabdomyolysis. Elevated CK may be due to direct cellular damage, decreased cellular metabolism, or a reversible defect in glycogenolysis. Although some publications suggest that the degree of hypothyroidism is correlated with elevated CK levels, no consistent correlation has been observed between the severity of symptoms and serum CK concentration (25,26). In a case report of a patient with severe hypothyroidism, it was reported that rhabdomyolysis and axonal neuropathy developed, and the very high CK level decreased to normal after hormone treatment. In hyperthyroidism, serum CK levels generally do not change (27-29).

CONCLUSION

Our study, in patient with thyroid dysfunction, the rate of neuromuscular complaints was higher than in the control group. PNP and CTS were higher in the hypothyroid patient group compared to the control group, while

PNP and CTS were not detected in the hyperthyroid patient group. Sural conduction velocity decrease or no SAP rate was higher in both patient groups. Our electroneurophysiologic studies have shown that sensorial nerve conduction velocity is affected before motor nerve conduction velocity in early thyroid dysfunction. Again, electroneurophysiologically, the percentage of myopathy was found to be higher in the hypothyroid patient group than in the hyperthyroid patient group and control. There was no statistical correlation between serum TSH, T3 and T4 levels and neuropathy and myopathy in both patient groups. Although serum CK concentration was not correlated with the degree of disease and myopathy, it was found to be significantly higher in hypothyroid patients.

Although the mechanism by which thyroid dysfunction affects the neuromuscular system is still debated. Neuromuscular symptoms may improve after treatment of thyroid disease. In future studies, comparison of post-treatment electrophysiologic values with pre-treatment values and clinical values may show the effect of thyroid function on the neuromuscular system more clearly.

DECLARATIONS

Ethics Committee Approval: This manuscript is retrieved from the graduation thesis of Arzu Akgül, MD, Ankara Numune Education and Research Hospital; 2003. Thesis no is 10548106. Dr. Erdal Eskioğlu was the Advisor of the thesis.

Financial Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions: AA; Project design, writing, and submitting, the other researchers equally contributed to data collection and analyzing the final version of the article. All authors read and approved the final manuscript.

Conflict of interest: None

Informed consent form: Not available

Funding source: No funding was received for the research

REFERENCES

1. Shahid MA, Ashraf MA, Sharma S. *Physiology, Thyroid Hormone.* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 [cited 2021 Jul 16]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK500006/
2. Örük GG., Bahçeci M. Tiroid ve paratiroid hastalıklarında nöromuskuler sistem bulguları. *Pam Tıp Derg*. 2013, 6(2):108-117.
3. Duyff RF, Van den Bosch J, Laman DM, van Loon BJ, Linssen WH. Neuromuscular findings in thyroid dysfunction: a prospective clinical and electrodiagnostic study. *J Neurol Neurosurg Psychiatry.* 2000;68(6):750-755. doi:10.1136/jnnp.68.6.750
4. Kececi H, Degirmenci Y. Hormone replacement therapy in hypothyroidism and nerve conduction study. *Neurophysiol Clin.* 2006;36(2):79-83. doi:10.1016/j.neucli.2006.04.001
5. Eslamian F, Bahrami A, Aghamohammadzadeh N, Niafar M, Salekzamani Y, Behkamrad K. Electrophysiologic changes in patients with untreated primary hypothyroidism. *J Clin Neurophysiol.* 2011;28(3):323-328. doi:10.1097/WNP.0b013e31821c30d9
6. Kumar N, Gadpayle AK, Roshan S. Thyrotoxic myo-neuropathy. J Indian Acad Clin Med. 13(3):255-6, 2012.
7. Papanikolaou N, Perros P. An unusual presenting symptom of graves' disease: myalgia. *Eur Thyroid J.* 2013;1(4):274-276. doi:10.1159/000343826
8. Cakir M, Samanci N, Balci N, Balci MK. Musculoskeletal manifestations in patients with thyroid disease. *Clin Endocrinol (Oxf).* 2003;59(2):162-167. doi:10.1046/j.1365-2265.2003.01786.x
9. Sözay S, Gökçe-Kutsal Y, Celiker R, Erbas T, Başgöze O. Neuroelectrophysiological evaluation of untreated hyperthyroid patients. *Thyroidology*. 1994 Aug;6(2):55-9.
10. El-Salem K, Ammari F. Neurophysiological changes in neurologically asymptomatic hypothyroid patients: a prospective cohort study. *J Clin Neurophysiol.* 2006;23(6):568-572. doi:10.1097/01.wnp.0000231273.22681.0e
11. Madhu SV, Jain R, Kant S, Prakash V, Kumar V. Myopathy presenting as a sole manifestation of hypothyroidism. *J Assoc Physicians India.* 2010;58:569-570.
12. Klein I, Levey GS. Thyroid myopathy. Thyroid Today. 1983;6:1–6.13
13. Akarsu EO, Acar H, Özer F, et al. Aşikar hipotiroidizm ve subklinik hipotiroidizmde elektromiyografik bulgular. *Turk Jour of Neurol.* 2013;19:128-133.
14. Donofrio PD, Albers JW. AAEM minimonograph #34: polyneuropathy: classification by nerve conduction studies and electromyography. *Muscle Nerve.* 1990;13(10):889-903. doi:10.1002/mus.880131002
15. Khedr EM, El Toony LF, Tarkhan MN, Abdella G. Peripheral and central nervous system alterations in hypothyroidism: electrophysiological findings. *Neuropsychobiology*. 2000;41(2):88-94. doi:10.1159/00002663820
16. Gupta N, Arora M, Sharma R, Arora KS. Peripheral and Central Nervous System Involvement in Recently Diagnosed Cases of Hypothyroidism: An Electrophysiological Study. *Ann Med Health Sci Res.* 2016;6(5):261-266. doi:10.4103/amhsr.amhsr_39_1621
17. Rao SN, Katiyar BC, Nair KR, Misra S. Neuromuscular status in hypothyroidism. *Acta Neurol Scand.* 1980;61(3):167-177. doi:10.1111/j.1600-0404.1980.tb01479.x
18. Kececi H, Degirmenci Y. Hormone replacement therapy in hypothyroidism and nerve conduction study. *Neurophysiol Clin.* 2006;36(2):79-83. doi:10.1016/j.neucli.2006.04.001
19. Nemni R, Bottacchi E, Fazio R, et al. Polyneuropathy in hypothyroidism: clinical, electrophysiological and morphological findings in four cases. *J Neurol Neurosurg Psychiatry.* 1987;50(11):1454-1460. doi:10.1136/jnnp.50.11.1454
20. Berlit P., Mahlberg U., Usadel KH. Polyneuropathy in hyperthyroidism-a clinical neurophysiologic study. *Schweiz Arch Neurol Psychiatr*.1992;143(1):81-90.
21. Suresh E, Morris IM. How valuable is screening for thyroid disease in patients with carpal tunnel syndrome?. J Clin Rheumatol. 2004;10(3):116-118. doi:10.1097/01.rhu.0000130859.10006.27
22. van Dijk MA, Reitsma JB, Fischer JC, Sanders GT. Indications for requesting laboratory tests for concurrent diseases in patients with carpal tunnel syndrome: a systematic review. *Clin Chem.* 2003;49(9):1437-1444. doi:10.1373/49.9.1437
23. de Rijk MC, Vermeij FH, Suntjens M, van Doorn PA. Does a carpal tunnel syndrome predict an underlying disease?. *J Neurol Neurosurg Psychiatry*. 2007;78(6):635-637. doi:10.1136/jnnp.2006.102145
24. Khaleeli AA, Griffith DG, Edwards RH. The clinical presentation of hypothyroid myopathy and its relationship to abnormalities in structure and function of skeletal muscle. *Clin Endocrinol (Oxf).* 1983;19(3):365-376. doi:10.1111/j.1365-2265.1983.tb00010.x
25. Finsterer J, Stöllberger C, Grossegger C, Kroiss A. Hypothyroid myopathy with unusually high serum creatine kinase values. *Horm Res.* 1999;52(4):205-208. doi:10.1159/000023462
26. Klein I, Ojamaa K. Thyroid (neuro)myopathy. *Lancet*. 2000;356(9230):614. doi:10.1016/s0140-6736(00)02601-5
27. Vold PL, Weiss PJ. Rhabdomyolysis from tourniquet trauma in a patient with hypothyroidism. *West J Med.* 1995;162(3):270-271.
28. Beyer IW, Karmali R, Demeester-Mirkine N, Cogan E, Fuss MJ. Serum creatine kinase levels in overt and subclinical hypothyroidism. *Thyroid*. 1998;8(11):1029-1031. doi:10.1089/thy.1998.8.1029
29. Brzozowska MM, Banthia S, Thompson S, Narasimhan M, Lee J. Severe Hypothyroidism Complicated by Myopathy and Neuropathy with Atypical Demyelinating Features. *Case Rep Endocrinol.* 2021;2021:5525156. Published 2021 May 19. doi:10.1155/2021/5525156