# Prevalence of Neuromuscular Abnormalities in Newly Diagnosed Patients with Thyroid Dysfunction

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## ABSTRACT

**Background:** Thyroid dysfunction is associated with characteristic symptoms, signs and functional alterations in many organs and systems. Central and peripheral nervous systems affection might provide the major presenting symptoms in a newly diagnosed of thyroid disease patients before starting treatment. The purpose of this study was to evaluate objectively the functional changes in the peripheral nervous system, muscles, and to determine the type and the prevalence of these diseases.
**Subjects and Methods:** A newly diagnosed 89 patients with thyroid dysfunction, which involved 58 with hypothyroidism and 31 with hyperthyroidism were included in this study. An additional, 42 persons with normal thyroid function were included as control group. The electrophysiological tests of nerve conduction and electromyography were achieved at the neurophysiology unit of the teaching hospital during the period Sep. 2010 through Oct. 2012 for both groups in parallel.
**Results:** In comparison to control group, and both hypo and hyperthyroid patients revealed deteriorated sensory conduction parameters worstly at lower limbs. The most commonly involved sensory fibers of the sural and median nerves were 43.1%, 39.6% in hypothyroid, respectively and 32.2% for both nerves in hyperthyroid patients, while sensorimotor neuropathies were less commonly seen 13.8% in hypothyroid and 3.2% in hyperthyroid patients. In electromyographic studies, the amplitude and duration of motor unit potentials in deltoid and abductor pollicis brevis muscles were performed, and myopathic changes mainly in the former muscle of the hypothyroid patients were recorded. In conclusion, revealed the early affection of the peripheral nervous system and muscles in the newly diagnosed thyroid patients pointing to the occurrence of the blamed hormonal and metabolic changes in an early disease course. Therefore, we suggest performing electrophysiological studies in those patients, even asymptomatic patients in an early course of disease before complications started.

**Key words:** Neuromuscular dysfunction, Thyroid dysfunction

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## INTRODUCTION

Variable manifestations usually revealed by endocrine diseases that may present with a wide variety of symptoms regarding different body organs and systems. This sometimes results in diagnostic delay; hence it is important for the clinician to be known the different neurological manifestations of endocrinopathies. Amongst various endocrine disorders, thyroid diseases are common in clinical practice [1,2]. Thyroid hormones are involved in many functions of the central and peripheral nervous system and as a result both hyperthyroidism and hypothyroidism may cause various neurological signs and symptoms [3]. The prevalence of neuromusculer disorders related to thyroid dysfunction has been reported to be between 20-80% [4]. More than one area may be affected but the brunt tends to be borne by some organ systems and this organ selectivity differs from one individual to another. It is also important to recognize that the neurological manifestations may be the presenting features and the other systems may be normal, to a large extent, at the time of presentation [5]. Two different types of peripheral nerve abnormalities are associated with established hypothyroidism. Although, the most common disorders are the entrapment neuropathies especially carpal tunnel syndrome (CTS), and sensorimotor polyneuropathies can also be seen in these patients [6]. The severity of the neuromuscular signs and symptoms are known to be related to the duration and degree of hormonal deficiency and clinical, electrophysiological and morphological improvement following hormone replacement therapy is typical [6,7]. Hyperthyroidism is less commonly associated with neuromuscular disorders and polyneuropathy is a relatively rare complication of hyperthyroidism [4,8]. The objectives of this study were to evaluate objectively the functional changes in the peripheral nervous system, muscles, and to determine the type and the prevalence of these diseases.

## SUBJECTS AND METHODS

One hundred thirty one subjects were included in this study. Of them, 58 with hypothyroidism, 31 with hyperthyroidism and 42 were free from thyroid dysfunction, which consider as a control group. T3 and T4 were tested for all participants to confirm the thyroid status. All participants were free from other disease, which could affect peripheral or central nervous system and a concept of participation in this study were taken from all. The participating patients were newly diagnosed and were not on any medication yet. This study was approved by ethical committee of faculty of medicine/ Kufa University. Students were explained the objective of this study and invited to participate. Consent form was obtained from the study participants.

The electrophysiological tests were achieved at the Neurophysiology Unit of the Teaching Hospital during the period of Sep. 2010 through Oct. 2012. Micromed NCS-EMG machine with all the required electrodes and accessories were used to do nerve conduction studies and electromyography for the patient and control groups in parallel.

Selected nerves of both upper and lower limbs were tested. The skin was adequately prepared before the application of the stimulating and recording electrodes, for both the sensory and motor nerve fibers measurements, to ensure good contact between these electrodes and the skin and to avoid any shock artifacts. This preparation included cleaning the skin by spirit and then drying. The electrodes were also prepared to ensure good conduction with subject's skin and to decrease skin impedance. These preparations included the soaking of the grounding electrodes, sensory recording electrodes, and felt tips of the stimulating electrode in normal saline. Electrode gel over the recording motor electrodes were also applied before being attached to the skin [9,10]. For both sensory and motor action potential recordings, the active recording electrode was placed proximal to the reference one, and for the stimulating electrodes, the anode was placed proximal to the cathode. Sensory latency, action potential amplitude and conduction velocity were recorded in the median, ulnar and sural nerves. Distal motor latency, compound muscle potential amplitude, conduction velocity and minimum F-wave latency were recorded in the median, ulnar and posterior tibial nerves.

The muscles examined were the right deltoid and abductor pollices brevis of all subjects. Using surface anatomy the muscle belly was identified and after disinfecting the skin overlying the muscle to be examined, implementation was performed by the needle electrode. The certainty of the electrode being inserted into the muscle is made by listening to the peculiar sound produced by the action potentials through the loud speaker. The potentials appear on the oscilloscope screen representing the insertion activity due to mechanical stimulation of the muscle fibers by the advancing electrode.

Multiple parameters were specifically looked for in the EMG examination, as spontaneous activity in relaxed muscle, twenty different motor unit potentials of each muscle were recorded and their average duration and amplitude were obtained, and the pattern of electrical activity during maximum contraction is also looked-for.

The statistical analysis was done using the Statistical Package for the Social Sciences (SPSS version 15), the arithmetic mean and standard deviation of distribution of each of the parameters were calculated for all of the subjects. The One Way ANOVA test was used to get the significance level (p-value) for all the patients parameters tested after

being compared with that of the control group. Chi- square test was used to determine the percentage and the significant level of the categorical variables. The T-test also used to get the mean ± SD of any parameter. A p-value equal to or less than 0.05 and 0.001 were considered to be significant and highly significant, respectively [10].

**RESULTS**

The characteristics of the 89 patients with thyroid dysfunction regarding their age, gender and their temperature were compared with control group (42 subjects). The results of age (mean ± SD) of hypo and hyperthyroid patients were 30.55±4.45, 32.05±6.45 and 34.97±5.05 respectively, that did not show statistically significant difference (p-value > 0.05). The number of the male participants was 16 (38.1%), 16 (24.6%) and 11 (35.5%), while that of the female participants was 26 (61.9%), 42 (72.4%) and 20 (64.5 %) for the control, hypo and hyperthyroid groups respectively showed no statistically significant difference (p-value > 0.05) between them and all participants had about the same body temperature of 36.89±0.27, 36.86±0.24 and 36.90±0.28 (in same sequence), which showed no significant difference.

**Nerve Conduction Findings**

The interested results of this study showed that the most sensory peripheral nerve in significant level (*p-value* <0.05). The highly significant level (*p-value* < 0.001) in parameter of latency (m.sec), especially in the median nerve showed in the hypothyroid compared to the hyperthyroid and control group, while sural nerve showed highly significant in both of hypothyroid and hyperthyroid compared to the control group. The amplitude (µvolt) showed highly significant levels in the median and sural in both of hypothyroid and hyperthyroid compared to the control group, while conduction velocity (m/sec) test showed highly significant of sural nerve in the hypothyroid patients only. On other hand, the motor parameters showed highly significant level (*p-value* < 0.001) of the conduction velocity (m/sec) test in the showed highly the median of hypothyroid cases compared to the hyperthyroid and control group (Table 1).

**Electromyographic Findings**

The Amplitude of deltoid muscles showed highly significant level (*p-value* < 0.001) in hypothyroid patients compared to hyperthyroid patients and control group (Table 2).

**Prevalence of Neuropathy in Thyroid Dysfunction Patients' Group**

Sensory neuropathy showed high prevalence in hypothyroid patients' group (44.8%) compared to the hyperthyroid patients' group followed by sural mononeuropathy (43.1%) and CTS (39.6%) (Table 3).

**Table 1: The sensory and motor conduction parameters of the tested median, ulnar, tibial and sural nerves within the control, hypothyroid and hyperthyroid patients' groups**

| **Parameters** (mean±SD) | | **Nerve** | **Control** | **Hypothyroid** | **Hyperthyroid** |
|---|---|---|---|---|---|
| Sensory | Latency (m.sec) | Median | 2.33 ± 0.51 | 2.80 ± 0.51 ** | 2.70 ± 0.51 * |
| | | Ulnar | 1.66 ± 0.28 | 1.71 ± 0.58 | 1.84 ± 0.31 |
| | | Sural | 1.76 ± 1.44 | 2.39 ± 0.49 ** | 2.35 ± 0.48 ** |
| | Amplitude (µvolt) | Median | 33.37±10.97 | 23.60 ±11.63 ** | 28.06 ± 8.88 * |
| | | Ulnar | 31.47±12.49 | 27. 34 ± 9.44 | 27.06 ± 10.61 |
| | | Sural | 23.85±4..91 | 17.63 ± 7.8 ** | 16.58 ± 7.08 ** |
| | Conduction Velocity (m/sec) | Median | 50.55 ± 7.21 | 44.37 ± 10.56 * | 46.38 ± 6.84 * |
| | | Ulnar | 55.14 ± 3.51 | 53.50 ± 4.34 * | 53.32 ± 2.95 * |
| | | Sural | 46.50 ± 3.39 | 41.39 ± 9.05 ** | 43.70 ± 7.85 |
| Motor | Distal Latency (m.sec) | Median | 2.91 ± 0.58 | 3.49 ± 1.23 * | 3.22 ± 0.83 |
| | | Ulnar | 2.10 ± 0.28 | 2.16 ± 0.35 | 2.06 ± 0.17 |
| | | Tibial | 3.06 ± 0.26 | 3.15 ± 0.36 | 3.12 ± 0.34 |
| | Amplitude (m. volt) | Median | 12.38 ± 3.08 | 10.14 ± 3.27 * | 11.70 ±5.14 |
| | | Ulnar | 5.96 ± 1.12 | 5.79 ± 1.16 | 5.87 ± 0.92 |
| | | Tibial | 5.02±1.17 | 5.25 ±1.75 | 5.37 ±1.63 |
| | Conduction Velocity (m/sec) | Median | 64.98±5.75 | 60.31±6.33 ** | 62.25±689 |
| | | Ulnar | 60.23 ± 6.00 | 58.31 ± 5.40 | 58.40 ± 5.47 |
| | | Tibial | 51.78±7.92 | 49.12±8.82 | 50.00±7.07 |
| | Minimal F-wave latency (m.sec) | Median | 24.29±2.39 | 26.18 ± 2.87 * | 25.64±3.19 * |
| | | Ulnar | 23.54 ± 0.80 | 24.06 ± 1.93 | 23.77 ± 1.74 |
| | | Tibial | 46.11±1.53 | 47.06±2.98 | 47.00±1.71 |

* = significant (*p-value* < 0.05); ** = highly significant (*p-value* < 0.001)

**Table 2: Some parameters of motor unit potentials of deltoid and APB muscles in control, hypothyroid and hyperthyroid patients' groups**

| **Parameter** (mean ± SD) | | **Control** | **Hypothyroid** | **Hyperthyroid** |
|---|---|---|---|---|
| Amplitude (µv) | Deltoid | 745 ± 181 | 560 ± 209 ** | 727 ± 212 |
| | APB | 742±174 | 725 ± 179 | 735 ± 181 |
| Duration (m sec) | Deltoid | 8.95 ± 1.61 | 8.10 ± 2.82 | 8.64 ± 1.89 |
| | APB | 8.89±1.94 | 8.25 ± 2.17 | 8.80 ± 1.94 |

APB= abductor pollicis brevis muscle; ** = highly significant (*p-value* < 0.001)

**Table 3: Prevalence of neuropathy in hypothyroid and hyperthyroid patients**

| **Findings** | **Hypothyroid** | **Hyperthyroid** |
|---|---|---|
| CTS | 23 (39.6%)) | 10 (32.2%) |
| Sural mononeuropathy | 25 (43.1%) | 10 (32.2%) |
| Sensory neuropathy | 26 (44.8%) | 11 (35.5%) |
| Sensorimotor polyneuropathy | 8 (13.8%) | 1 (3.2%) |

## DISCUSSION

The sensory latency of the median nerve was prolonged and the amplitude was decreased in hypothyroid and hyperthyroid patients (*P-value* <0.001 and <0.05) respectively when compared with the control group, findings that are consistent with that of Khedr *et al* [3]. The sensory conduction velocity of the median nerve in both hypothyroid and hyperthyroid patients was significantly decreased when compared with the control group, these results agreed with the results of other researchers [12]. The distal motor latency, motor amplitude and conduction velocity and F-wave minimal latency of the median nerve in hypothyroid patients was significantly changed when compared with the control group, these results agreed with Duyff *et al.,* and Brian and Bolton studies [4,12], and disagreed with others [13]. On another hand, in hyperthyroid patients, the results were not significant except the F-wave minimal latency, findings that were consistent that of Ozata, *et al* [13]. There was no significant alteration in ulnar nerve conduction parameters in both hypothyroid and hyperthyroid patients when compared with that of the control group, except the sensory conduction velocity in both patient groups that was significantly decreased, these results are in agreement with other researchers who found abnormal conductive parameters in ulnar nerve [14].

The sensory latency of the sural nerve was prolonged, the amplitude was decreased with decreased sensory conduction velocity (*P-value* <0.001) in both hypothyroid and hyperthyroid patients when compared with the control group, these results agreed with many researchers [3]. The conductive parameters of the tibial nerve (distal motor latency, motor conduction velocity and F-wave) in hypothyroid and hyperthyroid patients statistically were not significant when compared with the control group, these results are the same as that found by khedr *et al.,* and Tietgens *et al.,* [3,15].

In normal subjects, the electromyographic (EMG) study revealed that all motor unit potentials had normal shape of the potential. The parameters of the motor unit potentials and the interference pattern in all of them were perfectly normal. This is because neither insertion activity of long duration nor spontaneous muscle activities were noticed. This is in complete agreement with previous findings by other researchers [16]. Spontaneous activity was absent in both proximal and distal muscle, this does not agree with Scarpaezos *et al* [17] who reported these potentials in the APB of above 45 years old patients (a different age group might be the possible factor of this change from the readings of this study). However it was difficult to find absolute values for average amplitudes of the motor units in the literatures, which is probably due to the variability

of the amplitudes encountered during recording that is why we completely relay on the comparison between the patient and the control group. In the present study the mean amplitude of the deltoid in hypothyroid patients was significantly lower when compared with mean amplitude of this muscle in control subjects. This finding is in agreement with previous researchers who were able to demonstrate reduced amplitude of the motor unit potentials in proximal muscles of hypothyroid patients [5]. This finding of reduced amplitude of motor unit potentials can be considered as one of the evidences pointing out to myopathy, because in myopathy there is loss of muscle fibers and reduced fiber density. This suggests that hypothyroidism affects not only peripheral nerves but also the skeletal muscles, mainly the proximal ones. Regarding the duration of the motor unit there were no significant correlation in hypothyroid patients when compared with the control group. At the same time there were no significant EMG findings in hyperthyroid patients by comparing them with the control subjects and these findings agreed with Ozata *et al.,* [13] and disagreed with others [4].

It is known that thyroid hormones are involved in many processes and functions of the nervous system [18]. The severity of neuromuscular symptoms and signs correlates well with the degree and duration of hormonal imbalance [19] that might show the hormonal and metabolic changes which are responsible for the electrophysiological changes may occur early in the disease course before the diagnosis of the thyroid disease. The metabolic alteration caused by hormonal imbalance affects the Schwann cell, inducing demyelination that could be segmental. Primary axonal degeneration has also been shown electrophysiologically and affected initially, but later structural alterations may occur [12], Since the distal and sensory nerves are affected earlier [20], the most commonly involved nerves are the sural nerve and median nerve sensory fibers. There are 25 (43.1%) hypothyroid patients presented with sural mononeuropathy. Hypothyroidism slows metabolism, leading to fluid retention and swollen tissues that can exert pressure on peripheral nerves. Carpal tunnel syndrome (CTS) is caused by the deposition of mucinous material in the tissue surrounding the median nerve combined with hypothyroidism induced demyelinization [21]. The incidence of CTS varies and was reported in 5-92% of hypothyroid patients [3,20] and concluded that thyroid function tests were needed in all patients with carpal tunnel syndrome. The mucinous infiltrates found, by earlier researches, in the peripheral nerves could interfere mechanically with the metabolic exchange of nutrients and catabolic products to and from the neuron resulting in entrapment neuropathy. Some investigators found

morphological evidence of primary axonal degeneration. This could be explained by the energy deficit present in hypothyroidism, leading to decreased oxidation and the glycogen deposits due to its decreased degradation [8]. In hypothyroidism, the ATP deficiency and reduced activity of the ATP enzyme induce a decrease in $Na^+$-$K^+$ pump activity, with subsequent alterations of pump-dependent axonal transport which in turn leads to axonal neuropathy. This was supported by the study of Sidenius *et al.* [22] which demonstrated a reduced axonal velocity of slow component in sciatic nerves of hypothyroid rats, which is suggested to lead to axonal degeneration and peripheral neuropathy. Findings of this study were compatible with other researchers.

The prevalence of neuropathy in hyperthyroidism is less and the underlying mechanism for this is still unknown [3]. It has been suggested that in severe thyrotoxicosis, peripheral nerves are affected as well as dorsal root ganglion and anterior horn cells. In this study there was 10 (32.2%) hyperthyroid patients presented with sural mononeuropathy, where sural nerve was the most commonly involved nerve in this group of patients, and 10 (32.2%) of them had CTS. In previous studies that involved 141 of recently diagnosed untreated thyroid disease patients, 20% of the hyperthyroid patients were reported to have an axonal sensorimotor polyneuropathy [4,23].

## CONCULSIONS AND RECOMMENDATIONS

The prevalence of neuropathy in hyperthyroidism is lower than that in hypothyroidism and the involvement of the sensory nerves was more than that of the motor nerves and the affection of the lower limbs nerve fibers are worse than that of the upper limbs in both types of patients' groups. Furthermore, the sensory neuropathy, sural mononeuropathy and CTS represent the most common abnormalities in thyroid disease patients. Therefore, we have suggested performing electrophysiological studies in such patients early in the course of disease, even in asymptomatic cases in order to detect the possible abnormality to initiate treatment soon aiming to ameliorate symptoms and prevent complication.

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