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Subclinical Peripheral Nerve Affection in Hypothyroidism

Mai Abdelazeem, Abeer ElZohiery,Mona Elhussieny,Mohamed Ragaai
Physical Medicine, Rheumatology and Rehabilitation Department
Faculty of Medicine, Ain Shams University,Cairo, Egypt
*Corresponding author: Mai Abd Elazeem Abd Elazeem Rabie,Dr_mai_rabie@yahoo.com/01010999468

ABSRACT

Background: Hypothyroidism is most common endocrinal disorder. The existence of hypothyroid neuropathy is a point of debate and its pathogenesis is incompletely understood.

Objective: To detect subclinical motor or sensory peripheral nerve affection among hypothyroid patients.

Methods: The study was conducted on 30 hypothyroid patients without any neurological symptoms and signs. 10 healthy subjects were included as a control group. All participants were subjected to full medical history taking thorough clinical examination; full general and neurological examination, laboratory & radiological investigations and neurophysiologic nerve conduction study.

Results: The study revealed polyneuropathy, mainly sensorimotor, in 86.6% of the patients either axonal demyelination or axonal affection. Median and peroneal nerves were the dominantly affected nerves. High incidence of entrapment neuropathy was encountered among the patients especially carpal tunnel CTS (66.67%).**Conclusion:** Hypothyroidism is associated with polyneuropathy,mainly of a mixed type (axonal - demyelinating type).Nerve conduction tests should be performed routinely in hypothyroid patients early in the course of the disease, even among asymptomatic patients, to minimize structural damage and disability**.**

Key words: Hypothyroidism, nerve conduction study, neuropathy

INTRODUCTION

Thyroid hormones are involved in many processes and functions of the nervous system. They affect the central and peripheral nervous systems via their role in gene expression, production of myelin, and their effects on the neurotransmitter system and axonal transportation [(1).]

Hypothyroidism is a common medical condition in the general population caused by decreased hormone production leading to common systemic manifestations including fatigue, constipation, cold intolerance, weight gain, hair loss, dry skin, irregular menstrual periods and hoarseness[(2).]

Also, a variety of central and peripheral nervous system manifestations are common in patients with hypothyroidism like myxedema coma, cognitive impairment, cerebellar ataxia, carpal tunnel syndrome, tarsal tunnel syndrome, peripheral neuropathy, and mypathy[(3,4)]**.**

Diagnosis of hypothyroidism is based on laboratory testing:Elevated serum thyroid stimulating hormone (**TSH**) +/- low serum free thyroxine **(FT4**) concentration, +/- low serum free Triiodothyronine (**FT3**) concentration[(5).]

Peripheral neuropathy describes damage to the peripheral nervous system, which may affect sensation; movement, gland or organ function, and other aspects of health, depending on the type of nerve affected[(6).]

Peripheral neuropathy may be either inherited or acquired. Causes of acquired peripheral neuropathy include systemic diseases (the commonest cause), trauma from external agents, and infections or autoimmune disorders affecting nerve tissue. Neuropathy affecting just one nerve is called "mononeuropathy" and neuropathy involving multiple nerves in roughly the same areas on both sides of the body is called "symmetrical polyneuropathy" or simply "polyneuropathy". When two or more (typically just a few, but sometimes many) separate nerves in disparate areas of the body are affected it is called "mononeuritis multiplex"[(7)]**.**

The pathogenesis of the hypothyroid neuropathy is incompletely understood, with variable pathologic descriptions including mucopolysaccharide-protein complexes within the endoneurium and perineurium, reduction in the number of large myelinated fibers with segmental demyelination and remyelination, aggregates of glycogen granules, mitochondria, lipid droplets, and lamellar bodies and axonal degeneration with shrinkage of axons, and disruption of neurotubules and neurofilaments[(1).]

Nerve conduction studies (**NCS**) which include motor and sensory nerve conduction together with F wave study can play an important role in diagnosis of peripheral neuropathy because electrophysiological signs of neuropathy are

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detectable even sub clinically[6].

Objective of the study: To detect subclinical motor or sensory peripheral nerve affection among hypothyroid patients.

METHODS

This prospective study was conducted on 30 hypothyroidism patients with Elevated TSH +/- low serum free T4 concentration, +/- low serum free T3 concentration according to Dayan[5].

All patients were chosen randomly from those attending to obesity or endocrinology clinics outpatient clinics at Mataria Teaching Hospital. Ten healthy adult volunteers matched with patient group were included as a control group.

Exclusion criteria: Patients with diabetes, pregnant females, malignancies, renal failure, hepatic failure, hereditary sensory neuropathy, vitamin B12 or folate deficiency, hyperlipidemia, cervical or lumber radiculopathy, those on medications (contraceptive pills, drugs causing polyneuropathy or causing edema as steroids) or any other cause of PN were excluded from the study.

All participants were subjected to:

1. Full medical history taking: personal history**:** age, sex, and occupation, Present illness: complaint (with onset, coarse and duration), general symptoms related to hypothyroidism including fatigue, constipation, cold intolerance, weight gain, hair loss, dry skin, irregular menstrual periods and hoarseness, past history: DM, malignancies, radiations, thyroid surgery, fits, hepatic or renal disease and drugs, family history: Presence of malignancies, weakness and hereditary neuropathy and special habits: smoking, addiction and alcoholism.

2. Thorough Clinical Examination: General examination: focusing on pulse, arterial blood pressure (ABP), body weight, height and calculation of Body Mass Index (BMI) using the following equation: BMI=Weight (in Kilograms)/ height (in meters) ^{2} [8]. Full neurological examination was thoroughly done in details to detect any clinical sensory, motor, peripheral or central deficits.

3. Laboratory testing: TSH **,** free T4, free T3 ,Complete blood count (CBC), fasting blood sugar (FBS), post prandial blood sugar (PPBS), Kidney function tests, Liver function tests and lipid profile for exclusion criteria.

4. Plain x-ray on cervical and lumber spines was done for exclusion criteria.

5. Ethical committee: Consent was obtained from all patients and controls before the study after explaining all steps.

6. Electrophysiological nerve conduction studies: Electrophysiological studies were performed in a quiet room with a constant temperature set at 26 to31 ºC using thermostat of air condition. The patient was sitting or lying position, the procedure, purpose and importance of the test was fully explained to the patients prior to the test, the device used was Medtronic-Dantic Keypoint two channels (Medtronic Biomedica, Denmark-USA).

Tests done

A. Motor nerve conduction studies for median, ulnar , posterior, tibial and peroneal nerves were done according to Weiss [9]. Surface electrodes were used for both stimulation and recording. Stimulation was performed using supra-maximal stimulus (i.e. 20% higher than the intensity needed to get maximum amplitude of the recorded evoked motor response.

I. Median nerves: Active electrode (E1): was placed over of the abductor pollicis brevis. (Usually about half the distance from the distal wrist crease to the metacarpal phalangeal joint). **Referance electrode (E2):** was placed over the thenar tendons on the lateral surface of the thumb far from active electode at least 3 cm. **Ground electrode:** was placed over the dorsum of the wrist between the active electrode and the stimulator. **Stimulation** was done at the wrist distally between tendons of palmaris longus and flexor carpi radialis muscles; 8 cm proximal to the active, two stimulations were done. Distally at mid-palmar the stimulator is placed in the center of the palm over the crease formed by palmar abduction of the thumb and proximally, at elbow medial to tendon of biceps brachii muscle.

II. Ulnar nerve: Active electrode (E1): was placed over of the abductor digiti minimi, by palpating the muscle and abducting the 5th digit. **Referance electrode (E2):** was placed over the hypothenar tendons on the lateral surface of the little finger far from active electode at least 3 cm. **Ground electrode:** As median nerve**.** Stimulation:

1- At wrist, the stimulator was placed just medial to the flexor carpi ulnaris tendon 8 cm proximal to the active electrode.

2- *Below the elbow,* flex the elbow about 90 degrees, feel the ulnar groove and stimulate just below it.

3- *Above the elbow,* stimulation site is at least 10cm proximal to the below elbow stimulation in line

with the path of the ulnar nerve.

III. Posterior tibial nerve*:* **Active electrode (E1):** was placed over of the abductor hallucis muscle, by feeling the navicular bone of the foot just 1 finger breadth toward the plantar surface and 1 finger breadth toward the big toe. **Referance electrode (E2):** was placed on the big toe's medial surface. **Ground electrode:** was placed over the dorsum of the ankle. **Stimulation:** was done posterior to medial malleolus 10 cm proximal to the active electrode and then at the middle of the popliteal fossa.

IV. **Peroneal nerve: Active electrode (E1):** was placed on the center of extensor digitorum brevis (EDB) muscle by asking the patient to extend his toes and palpate for the muscle on anterior lateral surface of the dorsum of foot (usually located about 6 cm from the lateral malleolus). **Referance electrode (E2):** was placed over the lateral surface of the fifth digit. **Ground electrode:** As posterior tibial nerve. **Stimulation** was done at the ankle by measuring 8 cm proximal to EDB on the lateral anterior surface of foot then below fibular head and anterior to fibular neck, at thel popliteal fossa by Measuring 10 cm proximal from the fibula and stimulate in the lateral border of the popliteal fossa, Distal latencies, conduction velocities and amplitude of the evoked motor compound muscle action potentials were then calculated bilaterally. Values beyond normal limited were considered pathological according *to Preston and Shapir*o [(10)].

Table (1): Normal adult values of motor nerve conduction [(10).]

Nerve	Distal latency (ms)	Amplutide (mv)	Conduction Velocity(m/s)
Median	≤4.4	≥4.0	≥49
Ulnar	≤3.3	≥6.0	≥49
Posterior Tibial	≤5.8	≥4.0	≥41
Peroneal	≤6.5	≥2.0	≥44

F wave study: measuring mean latency

Same setups used for motor nerve conduction of individual nerves (median, ulnar, proneal and tibial). Stimulation positions the cathode proximal and use a supramaximal stimulus to the nerve using standard electrodeplacements. Normal values of mean f were <27 ms for median nerve, <29 ms for ulnar nerve, <52 for proneal nerve and<53 ms for tibial nerve beyond this normal limited were considered pathological according to Kimura [(11).]

B) Antidromic sensory nerve conduction study: It was done for median, ulnar, radial and sural nerves according to Weiss [(9).] **Threshold stimulus was used for stimulation of:**

I. Median nerve and radial nerve:

Ring surface electrodes applied to the thumb were used for recording with the active electrode over the metacarpophalangeal joint of the thumb and the reference electrode over the interphalangeal joint of the thumb. For the median nerve, stimulation was done at wrist (between flexor carpi radialis and palmaris longus) 10-12 cm proximal to the active electrode. As for the radial nerve, stimulation was done at the same distance but over the radial side of the forearm. Then, distal sensory latencies (latency to peak) of both nerves were calculated. Due to the identical distances from stimulating to recording electrodes over the same digit, thus, a peak latency difference exceeding 0.5 ms is suggestive of carpal tunnel syndrome [(12).]

II. Ulnar nerve

Ring surface electrodes applied to the little finger were used for recording with the active electrode over the metacarpophalangeal joint and the reference electrode over the interphalangeal joint. Stimulation was done at wrist 14 cm proximal to the active electrode near the crease of the wrist lateral to flexor carpi ulnarus.

III. Sural nerve

Active electrode was placed inferior to lateral malleolus about 1 cm and the reference electrode placed distal to active one about 3 cm. Stimulation was done 14 cm from active electrode near the middle line of calf muscle.

Measuring peak latency, amplitude and conduction velocity across the wrist of SNAP (sensory nerve action potential) was measured. Values beyond normal limited were considered pathological according to Preston and Shapiro [(10)].

Table (2): Normal adult value of sensory nerve conduction [(10).]

Nerve	Distal peak latency (ms)	Amplitude (μV)	Coduction velocity (m/s)
Median	≤3.5	≥20	≥50
Ulnar	≤3.1	≥17	≥50
Sural	≤4.4	≥6	≥40

- Diagnosing of early carpal tunnel syndrome by using advanced sensitive test

Mid palmar stimulation study: Motor nerve conduction study of median nerve while recording as usual from APB but stimulating the median

nerve 7 cm distal to the wrist site (on a line drawn from the median wrist to the web space between the index and middle fingers). Midpalm/wrist amplitude ratio of CMAP was determined Ratio > 1.6 considered abnormal and indicate element of conduction block [10].

Ethical committee

The study was done after approval of ethical board of Ain Shams University and informed written consent was taken from each participant in the study.

Demographic data: This study was conducted on thirty hyopthyroid patients and ten healthy matched subjects serving as a control group. The patients were 27 females (90.0%) and 3 males (10.0 %) with a female to male ratio of 9: 1. Their ages ranged from 16 years to 55 years with mean age of 36.1±10.3 years. Their BMI ranged from 17.1 to 30 with a mean of 25.1±4.0.While, the control group was 9 females (90.0%) and 1 male (10.0%) with a female to male ratio of 9:1. Their ages ranged from 22 years to 43 years with a mean of 34.3±7.1 years. Their BMI ranged from 17.2 to 28 with a mean of 22.9±3.8.

RESULTS

(I) Clinical Data:

1- ***Laboratory data***

Table (3): Comparison between patients and controls as regards thyroid profile

Varaible	Measure	Patient (N=30)	Control (N=10)	T	P	Sig.
TSH (mIU/L)	**Mean±SD**	6.0±2.2	2.2±0.6	4.818	**<0.001**	**S**
FT3 (mcg/dl)	**Mean±SD**	1.9±0.9	2.4±0.5	1.445	0.157	NS
FT4 (nmol/L)	**Mean±SD**	3.1±0.8	7.4±2.1	4.488	**<0.001**	**S**

Independent t-test, S: significance, NS: no significance, SD: standard deviation

No significant difference between study groups regarding **FT3**, while **FT4** was significantly lower among patient group than control group and **TSH** was significantly higher among patient group than control group and (P >0.05).

Nerve conduction studies

a) Results of motor nerve conduction study:.

Table (4): Comparison between patients and controls as regards motor nerve conduction study of both median nerves

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
DML (ms)	**Rt**	3.5±0.5	3.0±0.3	3.169	0.003	**S**
	Lt	3.6±0.8	2.9±0.5	2.386	0.022	**S**
Median W Amplitude (mv)	**Rt**	8.0±1.8	10.4±1.9	3.716	<0.001	**S**
	Lt	8.6±2.0	10.4±3.2	2.130	0.040	**S**
Median MP Amplitude (mv)	**Rt**	9.4±2.0	10.9±1.6	2.112	0.041	**S**
	Lt	9.7±2.1	10.6±3.3	1.079	0.288	NS
Median E Amplitude (mv)	**Rt**	8.2±2.5	11.1±1.8	3.336	0.002	**S**
	Lt	8.4±1.8	10.5±3.0	2.631	0.012	**S**
NCV (m/s)	**Rt**	56.5±4.0	60.9±2.6	3.271	0.002	**S**
	Lt	57.3±3.6	62.6±2.8	4.185	<0.001	**S**
Mean. F-M Lat. (ms)	**Rt**	24.4±1.8	24.3±1.2	0.116	0.908	NS
	Lt	23.4±1.8	24.0±0.8	0.911	0.368	NS

Independent t-test, S: significance, NS: no significance,**DML:** distal motor latency,**W:** wrist,**MP:** Mid palma. **E:** elbow,**NCV:** nerve conduction velocity, **lat:** latency

There was a statistically significant difference between patients and controls as regards DML, wrist, elbow and right MP amplitude and NCV of both median nerve (P<0.05). There was no statistically significant difference between patients and controls as regards left MP amplitude and mean F-M latencies in both median nerves (P>0.05).

Table (5): Comparison between patients and controls as regards motor nerve conduction study of both ulnar nerves

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
DML (ms)	**Rt**	2.5±0.2	2.4±0.3	1.229	0.227	NS
	Lt	2.7±0.4	2.3±0.3	2.734	0.009	**S**
Ulnar W Amplitude (mv)	**Rt**	8.7±2.5	10.6±2.3	2.060	0.046	**S**
	Lt	8.6±1.6	10.0±2.0	2.359	0.024	**S**
Ulnar E Amplitude (mv)	**Rt**	8.1±2.3	9.9±2.6	2.093	0.043	**S**
	Lt	7.5±1.3	9.7±2.4	3.600	<0.001	**S**
NCV Wrist (m/s)	**Rt**	59.1±4.7	62.6±3.3	2.121	0.041	**S**
	Lt	58.1±4.8	61.8±3.9	2.236	0.031	**S**
NCV Elbow (m/s)	**Rt**	59.1±4.7	62.6±3.3	2.167	0.038	**S**
	Lt	58.4±4.7	61.8±3.9	2.073	0.045	**S**
Mean. F-M Lat. (ms)	**Rt**	25.1±2.1	25.8±1.9	0.972	0.337	NS
	Lt	24.6±2.0	25.0±1.3	0.604	0.550	NS

There was a statistically significant difference between patients and controls as regards DML, amplitude at wrist& elbow and NCV at wrist &elbow of both ulnar nerves (P<0.05). There was no statistically significant difference between patients and controls as regards mean F-M latencies in both ulnar nerves (P>0.05).

Table (6): Comparison between patients and controls as regards motor nerve conduction study of both posterior tibial nerves.

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
DML (ms)	**Rt**	4.5±1.0	3.7±0.4	2.433	0.020	**S**
	Lt	5.2±1.1	3.7±0.5	4.125	<0.001	**S**
Amplitude (mv)	**Rt**	8.7±2.0	12.1±3.0	3.111	0.004	**S**
	Lt	8.0±2.4	12.1±2.8	4.457	<0.001	**S**
NCV (m/s)	**Rt**	48.9±6.2	53.1±2.6	2.148	0.042	**S**
	Lt	47.0±3.7	52.3±1.5	4.365	<0.001	**S**
Mean. F-M Lat. (ms)	**Rt**	44.0±4.1	43.8±0.9	0.135	0.893	NS
	Lt	43.0±6.4	43.2±0.7	0.073	0.942	NS

There was a statistically significant difference between patients and controls as regards DML, amplitude and NCV of both posterior tibial nerves (P<0.05). There was no statistically significant difference between patients and controls as regards mean F-M latencies and right DML in both posterior tibial nerves (P>0.05).

Table (7): Comparison between patients and controls as regards motor nerve conduction study of peroneal nerves.

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
DML (ms)	**Rt**	3.9±0.7	3.4±0.4	2.215	0.033	**S**
	Lt	4.1±0.7	3.4±0.3	3.238	0.003	**S**
Peroneal A Amplitude (v)	**Rt**	4.0±2.0	6.9±0.7	4.533	<0.001	**S**
	Lt	3.3±1.5	4.7±0.6	2.810	0.008	**S**
Peroneal K Amplitude (mv)	**Rt**	3.1±1.4	4.9±0.4	4.013	<0.001	**S**
	Lt	3.1±1.6	4.6±0.7	2.953	0.005	**S**
NCV Ankle (m/s)	**Rt**	47.7±3.2	49.9±0.7	2.109	0.038	**S**
	Lt	48.9±3.4	51.4±1.1	2.227	0.032	**S**
NCV Knee (m/s)	**Rt**	47.6±5.3	53.9±1.8	2.152	<0.001	**S**
	Lt	50.7±6.3	55.3±2.3	2.258	0.030	**S**
Mean. F-M Lat. (ms)	**Rt**	41.4±7.2	44.0±0.7	1.109	0.274	NS
	Lt	40.7±5.2	41.8±0.8	0.699	0.489	NS

T

here was a statistically significant difference between patients and controls as regards DML, amplitude at ankle& knee and NCV at ankle &knee of both peroneal nerves (P<0.05). There was no statistically significant difference between patients and controls as regards mean F-M latencies in both peroneal nerves (P>0.05).

b) Results of sensory nerve conduction study:

Table (8): Comparison between patients and controls as regards sensory nerve conduction study of both median nerves.

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
DSL (ms)	**Rt**	2.7±0.5	2.3±0.3	2.355	0.024	**S**
	Lt	2.9±0.7	2.4±0.2	2.066	0.046	**S**
Amplitude (mv)	**Rt**	17.6±6.8	25.2±3.8	3.35	0.002	**S**
	Lt	19.3±5.6	25.0±3.0	3.08	0.004	**S**
NCV (m/s)	**Rt**	47.2±7.2	60.9±5.4	5.498	<0.001	**HS**
	Lt	47.6±9.7	62.5±2.2	4.78	<0.001	**HS**

There was a statistically significant difference between patients and controls as regards DSL, amplitude and highly significant NCV of both median nerves (P<0.05).

Table (9): Comparison between patients and controls as regards distal sensory latency of both median and radial nerves

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
Median DSL (ms)	**Rt**	2.7±0.5	2.3±0.3	2.355	0.024	**S**
	Lt	2.9±0.7	2.4±0.2	2.066	0.046	**S**
Radial DSL (mv)	**Rt**	2.74 ± 0.50	2.53 ± 0.51	3.35	0.002	**NS**
	Lt	2.71 ±0.48	2.56 ± 0.64	3.08	0.004	**NS**

There was statistically significant difference between patients and controls as regards mean values of distal sensory latencies of both median (P<0.05). While there was no statistically significant difference between patients and controls as regards mean values of distal sensory latencies of both radial nerves (P>0.05).

Table (10): Comparison between median and radial mean DSL of the patients.

Function	Side	Median (N=30)	Redial (N=10)	T	P	Sig.
DSL (ms)	**Rt**	3.05 ± 0.57	2.74 ± 0.50	2.228	0.030	**S**
	Lt	3.01 ± 0.59	2.71 ± 0.48	2.114	0.039	**S**

Patients showed statistically significant higher mean distal sensory latencies in both median nerves than both radial nerves (P<0.05).

Table (11): Comparison between patients and controls as regards sensory nerve conduction study of both ulnar nerves.

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
DSL (ms)	**Rt**	2.4±0.3	2.3±0.2	0.99	0.327	NS
	Lt	2.4±0.3	2.3±0.2	1.29	0.203	NS
Amplitude (mv)	**Rt**	17.4±6.6	25.7±8.4	3.236	**0.003**	**S**
	Lt	21.3±8.3	32.1±3.9	3.948	**<0.001**	**HS**
NCV (m/s)	**Rt**	54.8±6.6	60.1±4.1	2.344	**0.024**	**HS**
	Lt	56.8±5.2	61.9±3.7	2.856	**0.007**	**HS**

There was statistically significant difference between patients and controls as regards mean values of RT amplutide and highly significant with it amplitude and NCV of both ulnar (P<0.05).While there was no statistically significant difference between patients and controls as regards mean values of distal sensory latencies of both ulnar nerves (P>0.05).

Table (12): Comparison between patients and controls as regards sensory nerve conduction study of both sural nerves.

Function	Side	Patient (N=30)	Control (N=10)	T	P	Sig.
Latency (ms)	**Rt**	3.5±0.6	3.0±0.4	2.545	0.015	**S**
	Lt	3.8±1.1	3.0±0.4	2.281	0.028	**S**
Amplitude (mv)	**Rt**	14.6±6.7	22.6±3.9	3.581	**<0.001**	**S**
	Lt	12.6±7.3	21.3±3.2	3.647	**<0.001**	**HS**
NCV (m/s)	**Rt**	53.4±11.0	67.2±2.3	3.910	**<0.001**	**HS**
	Lt	48.2±11.3	66.7±1.9	5.119	**<0.001**	**HS**

There was statistically significant difference between patients and controls as regards mean values of distal sensory latencies and RT amplitude, highly significant with LT amplitudes and NCVs of both sural nerves. (P<0.05)

Table (13): Types of neuropathies among our patients

Nerve	N	%
According to number affected		
Mononeuropathy	0	0
Polyneuropathy	26	86.6
Normal	4	13.4
According to type		
Motor neuropathy	0	0
Sensory neuropathy	11	42.3
Sensorimotor	15	57.7

Total=30 cases, N: number of cases

Table (13) shows that 86.6% of our patients had polyneuropathy.13.4% were normal & none of our patients showed mononeuropathy. Also, 42.3% of our patients had pure sensory neuropathy, 57.7% had sensorimotor neuropathy & none had pure motor neuropathy.

Table (14): Distribution of affected nerves among our patients

Nerve	N	%
Motor nerves		
Median	16	26.7
Ulnar	12	20.0
Peroneal	25	41.7
Tibial	15	25.0
Sensory nerves		
Median	49	81.7
Ulnar	20	33.3
Sural	19	31.7

Total=60 lateral nerves, N; number of affected nerve (156)

Table (**14**) shows that the median nerve & the peroneal nerve were more commonly affected (81.7%, 41.7% respectivly) while the other affected nerves represented as sensory ulnar nerve (33.3%), sural nerve (31.7%), motor medin nerve (26.7), tibial nerve (25%) and motor ulnar nerve (20%).

Table (15): Pathological affection in sensorimotor neuropathy.

A) Motor nerves (43.6%)		
Pathology	**N**	**%**
Demylination	9	5.8
Axonal	22	14.1
Mixed	37	23.7
B) Sensory nerves (18.6%)		
Demylination	4	2.6
Axonal	12	7.7
Mixed	13	8.3

N: number of affected nerves (156)

Table (**15**) shows that the mixed sensorimtor affection was the most dominant, affecting motor nerves 23.7% & sensory nerves 8.3%, while axonal affection was 14.1% in motor nerves & 7.7% in sensory nerves and demylinating affection was 5.8% in motor nerves & 2.6% in sensory nerves.

Table (16): Pathological affection in sensory neuropathy

Pathology	N	%
Demylination	10	16.9
Axonal	34	57.6
Mixed	15	25.42

N: number of affected nerves (156)

Table (**16**) shows that the axonal affection was the most represented in sensory neuropathy 57.5% while mixed affection was 25.42% and demylinating affection was 16.9%.

Table (17): Nerves exceeding the upper normal limit of DML

DML (ms)	Normal Limit	Right		Left		Bil.		Total number of patients	
		N	%	N	%	N	%	N	%
Median	≤4.4	1	3.3	2	6.7	1	3.3	2	6.7
Ulnar	≤3.3	0	00	3	10	0	00	3	10
tibial	≤5.8	2	6.7	7	23.33	2	6.7	7	23.33
Peroneal	≤6.5	0	00	0	00	0	00	00	00

N: number of nerves

Table (18): Nerves exceeding the upper normal limit of DSL

DSL (ms)	Normal Value	Right		Left		Bil.		Total number of patients	
		N	%	N	%	N	%	N	%
Median	≤3.5	2	6.7	2	6.7	1	3.3	3	10
Ulnar	≤3.1	0	00	0	00	0	00	0	00
Sural	≤4.4	2	6.7	2	6.7	1	3.3	3	10

N: number of nerves

According to table (17) & table (18) patients with CTS were eleven cases had bilateral CTS and nine cases had unilateral CTS, thus giving a total of 20 cases CTS (66.67%). Patient with TTS were two cases had bilateral TTS and five cases had unilateral TTS, thus giving a total of seven cases TTS. Patient with cubital tunnel were two cases bilaterally, diagnosed by slowing of above and below elbow conduction velocity for more than 10 meters/second on the same side, three patients had unilateral ulnar entrapment neuropathy and 3 cases had sural neuropathy by exceeding DL.

DISCUSSION

In the present study, the comparison of age and BMI of control and hypothyroid groups did not reveal any significant difference, as the groups were matched in age and BMI. On the other hand, ***Karne and Bhalerao*** [13] found the prevalence of peripheral neuropathy was 8% in persons 55 years and older, proving that neuropathy increases as age advances**.** They also mentioned the same correlation between high BMI and neuropathy in hypothyroidism. This difference might be owed to their enrollment of many patients above the age 55. Besides, 25% of their samples were obese.

In the current work, polyneuropathy was evident in 86.6% of our patients & none of them showed mononeuropathy. Also, 57.7 % had sensorimotor neuropathy, 42. 3% had sensory neuropathy & none had pure motor neuropathy.

The type of neuropathy detected among hypothyroid patients has been a point of debate among several previous studies. Sensory-motor polyneuropathy was the predominant finding in many studies [14, 15, 16, 17].

On the other hand, pure sensory polyneuropathy was the main outcome finding by others [18, 13, 19].

Moreover, ***Ajeena*** [20] detected high prevalence of sensory neuropathy (44%), followed by sural mononeuropathy (43%).

In addition Balaraman ***et al.*** [21] found a significant reduction in sensory nerve conduction (latency, amplitude, duration, area, conduction velocity) in median and sural nerves as well as 10% purely motor neuropathy.

It could be noticed that though there are minor dissimilarities between the different studies, yet, the corner stone outcome is sensorimotor & sensory neuropathy among hypothyroid cases, a finding that we too have confirmed.

The variations could depend on many factors as duration of diseases, treated or not, dose of Eltroxin & proper control as well as patient age and BMI.

The commonest pathological presentation in our study was sensorimotor axonal –demylination followed by sensory axonal then least likely demylination neuropathy.

This presentation was similarly encountered in few recent studies [1, 22, 13, 14]

Instead, ***Duyff et al.*** [14] detected that pure axonal sensorimotor was a predominant finding among their patients. On the other hand, ***Asia and***

Warkar [19] mentioned that sensory demyelinating polyneuropathy was commonly encountered in their study.

Thyroid hormones have profound effects on mitochondrial oxidative activity, synthesis and degradation of proteins and sensitivity to catecholamines. Neural development interacts with a variety of important growth factors and may modulate axonal growth through regulation of microtubule assembly. This may suggest a possible mechanism for axonal degeneration.

In our present study, the most two affected nerves were median nerve and proneal nerve. This finding matched with ***Waghmare et al.*** [1] who found abnormal nerve conduction studies in hypothyroid patients predominantly affecting peroneal and median nerves. On the other hand, ***Beghi et al.*** [18] reported that sural nerves followed by median sensory were more predominant. This may be due to different electrophysiological protocols used in the two studies. As we used median-versus-radial sensory comparison test for early detection of sensory median nerve entrapment while they used the antidromic median nerve study from the middle finger using surface electrode.

We detected 66.67% of CTS among our patients, a finding that was commonly encountered by ***Karne and Bhalerao*** [13] ***and Cruz et al.*** [23] who found 60% & 71.42% of their patients having CTS respectively.

On the other hand, ***Ajeena*** [9] and ***Asia & Warkar*** [19] didn't establish the same high percent. This again could be due to the different neurophysiological methodology used. We used the sensitive median-versus-radial sensory comparison test and mid palmar stimulation study besides the conventional tests for diagnosing CTS. On the other hand, they only depended upon the antidromic median nerve study from the middle finger using surface electrode to diagnose CTS.

As for the motor finding in the present study**,** there was a statistically significant difference between patients and controls as regards DML, distal amplitude and NCV of both median, tibial and proneal nerves ($P<0.05$)**.**This finding agrees with ***Waghmare et al.*** [1] ***Ashwini et al.*** [22] ***and Somay et al*** [16] who found significant difference between patients and control groups regarding DML, CMAP and CV predominantly affecting median and proneal nerves. This finding disagrees with ***Balaraman et al.*** [21] ***Asia& Warkar*** [19] and ***Jalilzadeh***[24] who found no statistically significant difference between patients and controls as regards all motor parameters. This discrepancy might be attributed to having all their patients newly diagnosed.

In the present study, no significant difference was noted between patient and control group's median, ulnar, tibial and peroneal nerves F wave studies. A similar finding was seen by ***Udayakumar et al.*** [25] and ***Balaraman et al.*** [21] who had found no significant difference between their patients and control groups for median and peroneal nerves F wave parameters. This outcome somehow excludes a proximal nerve lesion, radiculopathy or plexopathy**.** However, it isn't a sensitive test, though a good positive test, yet, not a good negative test [26]**.**

During our work, we noticed that 13.4% of hypothyroid patients showed no abnormal electrophysiological findings, which is compatible with ***Jalilzadeh*** [24] who found normal electrophysiological findings in subclinical hypothyroidism. That was referred to the pathogenetic basis of alterations in peripheral nerve function in hypothyroidism, which is reversible with thyroxine replacement therapy. In subclinical hypothyroidism serum free thyroxine levels are maintained within normal limits by elevated TSH concentrations. Thus, it may be reasonable to find no significant impairment in peripheral nerve function in subclinical hypothyroidism. So, this percentage with normal findings may be reflecting those patients with subclinical hypothyroidism.

This result agreed with ***Yeasmin et al.*** [27] who found no significant correlations between the thyroid hormones and most of the nerve conduction parameters of the median, ulnar, peroneal and sural nerves and he suggested that it may be due to the almost normal values of TT3 and TT4 in his hypothyroid subjects as most of them were on hormone therapy and the thyroid deficiency may be a factor for the deterioration of nerve conduction parameters.

To sum up our work, polyneuropathy on hypothyroidism is mainly sensorimotor, in 86.6% of the patients either axonal demyelination or axonal affection. Median and peroneal nerves were the dominantly affected nerves. High incidence of entrapment neuropathy was encountered among the patients especially CTS (66.67%).

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