Original Research Article

Evaluation of prevalence of neuromuscular disorders in thyroid disorders in tertiary care institution - An interdepartmental inter institutional study

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Abstract

Background: The prevalence of Neuromuscular disorders in thyroid disorders is reported to be from 20% to 60% and varies from neuropathy to proximal myopathy. This study attempts to evaluate the prevalence of neuromuscular disorders in thyroid disorders.

Aim and objectives: To study the correlation and prevalence of Nerve conduction abnormalities in hypothyroidism and hyperthyroidism, to determine neuropathy and myopathy in subsect of patients with thyroid disorders.

Materials and methods: This study setting was in tertiary medical care centres which are major teaching institutes confined to the same geographical zone with a similar type of patient inflow. The departments of Medical endocrinology Out Patient patients and Endocrine surgery along with Internal medicine were included to evaluate patients. All patients were subjected to evaluation by Neurologist, Endocrine surgeons, Physician and Nuclear Physician. A total number of 400 patients over a period of three years were included from 2015 till 2018 with one year follow-up after treatment. The inclusion

criteria were newly detected thyroid dysfunction predominantly hypothyroidism and hyperthyroidism and a subset of patients refractory to medical treatment where intervention was total thyroidectomy. The exclusion criteria were toxic nodules, thyroiditis, unmarried girls and postoperative disease states. All Patients were subjected to a questionnaire and nerve conduction study was performed using standard RMS ENMG EP Mark Ii Machine to derive results for comparative analysis.

Results: Out of the 400 patients studied 144 had neuropathy of which 4 patients had hyperthyroidism and 56 had hypothyroidism. 8 patients had mononeuropathy and 64 had polyneuropathy. Proximal Myopathy was present predominantly in hyperthyroidism especially Graves' disease.

Conclusion: The outcome of the evaluation in the study revealed that hypothyroid patients predominantly had Neuropathy and Hyperthyroidism patients had proximal Myopathy especially in Graves' disease. The commencement of hyperthyroidism especially in Graves' Disease is significant along with commencement of therapy to assess the progression of proximal Myopathy which is prevalent three fold in Graves Disease than in hyperthyroidism.

Key words

Hypothyroidism, Hyperthyroidism, Nerve conduction, Myopathy, Neuropathy.

Introduction

Thyroid dysfunction is associated with hypothyroidism and hyperthyroidism. Thyrotoxicosis is the result of excess thyroid hormone production from anywhere but thyrotoxicosis is over production of thyroid hormones from within the thyroid gland only [1]. Both hypothyroidism and hyperthyroidism may cause signs and symptoms of neuromuscular dysfunction. Hypothyroidism is associated with peripheral nerve demyelination and decreased nerve conduction velocity [2]. In adults with newly diagnosed hypothyroidism, neuromuscular abnormalities including neuropathy occur commonly and have long been recognized, with up to half experiencing signs of sensorimotor neuropathy; of these, carpal tunnel syndrome appears to be particularly common [3]. Mucinous infiltration of the perineurium and endoneurium occur in hypothyroid patients with carpal tunnel syndrome [4]. Neurophysiological studies show that polyneuropathy is frequent, with decreased nerve conduction velocity and fibrillation potentials occurring frequently in adults with primary hypothyroidism [5]. In adults, the most common finding is sensory loss, usually bilateral and distal, and may be augmenting classical glove-and-stocking distributionif there is impaired glucose tolerance [6]. Deep tendon reflexes show a delayed relaxation phase, a classical sign on physical examination of acquired primary hypothyroidism, which is seen in children and adolescents with new-onset or severe primary hypothyroidism [7]. However, minimal data are available in children to document the prevalence of neuropathy. Equally, it is unclear in children whether normalization of circulating thyroid hormone levels prevents the onset of peripheral neuropathy, or whether neuropathy resolves after initiation of thyroid hormone replacement [8]. In an adult series, symptoms of neuropathy may be present for months or years before a diagnosis of hypothyroidism is confirmed. Although the clinical and electrophysiological changes significantly normalize in adults treated with thyroid hormone replacement, those with a longer duration of symptoms (and thus, presumably, more nerve damage) have a higher chance of persistent symptoms and signs of peripheral neuropathy [9].

Materials and methods

This study setting was in tertiary medical care centres which were major teaching institutes confined to the same geographical zone with similar type of patient inflow. The Departments of Medical Endocrinology and Endocrine Surgery along with Internal Medicine were included to evaluate patients and subsequently

subjected to evaluation by neurologist, endocrine surgeon, physician and nuclear medicine specialist. A total number of 400 patients over a period of three years were included from 2015 till 2018 with one year followup after treatment. The inclusion criteria were newly detected thyroid dysfunction predominantly hypothyroidism and hyperthyroidism and a subsect of patients refractory to medical treatment where intervention was total thyroidectomy. The exclusion criteria were toxic nodules, thyroiditis, unmarried girls and post operative disease states. All patients were subjected to a questionnaire and nerve conduction study was performed using standard RMS ENMG EP MARK II MACHINE to derive results for comparative analysis.

Results

The baseline range and the thyroid function values were given in **Table - 1**. Out of the 400 patients studied 144 had neuropathy of which 4 patient had hyper thyroidism and 56 had hypothyroidism. 8 patients had mono neuropathy and 64 had polyneuropathy. Proximal Myopathy was present predominanty in hyperthyroidism especially Graves' disease (**Table – 2 to 6**).

Table – 1: Hyper and hypothyroidism prevalence in the study based on TSH, free T4 and T3.

Thyroid Parameters		**TSH (uU/mL)**	**Free T4 (ng/dL)**	**Free T3 (ng/dL)**
All	N	400	400	400
	Mean	19.96	3.39	5.41
	SD	26.05	5.58	6.98
Hypothyroid	N	37	37	37
	Mean	26.63	0.61	1.88
	SD	27.31	0.22	0.50
Hyperthyroid	N	13	13	13
	Mean	0.99	11.27	15.46
	SD	2.69	5.99	7.12

Table – 2: Neuromuscular conduction studies were carried out to all patients and the CMAP was plotted.

CMAP (Amplitude) (mv)		**Right Median**	**Left Median**	**Right Ulnar**	**Left Ulnar**	**Right Peroneal**	**Left Peroneal**	**Right Tibial**	**Left Tibial**
All	N	400	400	400	400	400	400	400	400
	Mean	15.32	13.52	10.62	9.95	6.47	6.69	13.99	14.46
	SD	11.50	4.57	2.46	2.31	2.32	2.14	5.34	5.11
Hyperthyroid	N	37	37	37	37	37	37	37	37
	Mean	15.58	13.90	10.66	9.81	6.71	6.93	14.30	14.36
	SD	12.94	4.58	2.37	2.30	2.44	1.98	5.62	5.25
Hypothyroid	N	13	13	13	13	13	13	13	13
	Mean	14.58	12.43	10.52	10.36	5.78	6.01	13.10	14.74
	SD	5.08	3.52	2.42	2.08	1.42	2.12	4.12	4.48
P value Unpaired 't'		0.0140	0.0253	0.0168	0.0411	0.0027	0.0479	0.0493	0.0169

Discussion

Excess thyroxine is believed to bring about the onset of thyrotoxic myopathy and eventually cause the degradation of muscle tissue. Thyroxine is a hormone produced in the thyroid gland that regulates the growth metabolism of the nervous system and regulates basal metabolic rate of many cell types [10]. Scientists agree thyroxine brings about the degradation of muscle fibers specifically at the motor end plates of neuromuscular junctions. There is debate as to whether thyroxine degrades the motor end plates from the muscular side, from the nervous system side, or a combination. Abnormal thyroid

function, either too much or too little, can cause myopathy [11]. With the onset of TM due to thyroxine toxicity, there is evidence to suggest that structural changes in MEPs could lead to muscle fiber degradation, weakness, and fatigue. Research indicates that decreased levels of Acetylcholinesterase AChE, an enzyme that breaks down ACh, was observed within the neuromuscular junction. This decrease in AChE blocks degradation of ACh causing ACh to increasingly stimulate the MEP of the muscle fiber. Over stimulation of MEP could cause more muscle contractions which eventually evoke muscle fiber fatigue, weakness, and finally degradation, which are characteristic symptoms of TM [12].

Table – 3: The distribution pattern in upper and lower limb nerves employing m NCV.

MNCV (m/s)		**Right Median**	**Left Median**	**Right Ulnar**	**Left Ulnar**	**Right Peroneal**	**Left Peroneal**	**Right Tibial**	**Left Tibial**
All	N	400	400	400	40	400	400	400	400
	Mean	58.58	58.88	58.25	61.82	44.38	43.93	52.87	50.30
	SD	5.86	6.02	5.56	7.14	4.28	6.86	23.07	10.76
Hypothyroid	N	37	37	37	37	37	37	37	37
	Mean	59.46	59.76	59.05	63.05	44.60	42.90	54.94	50.74
	SD	6.16	6.47	5.17	7.61	4.41	7.44	26.42	12.16
Hyperthyroid	N	13	13	13	13	13	13	13	13
	Mean	56.08	56.39	55.99	58.31	43.72	46.88	46.97	49.06
	SD	4.17	3.67	6.22	4.08	3.99	3.68	5.33	5.18
P value Unpaired 't'		0.1354	0.2277	0.1288	0.3378	0.5122	0.4162	0.0896	0.5002

Table – 4: The f wave were compared and tabulated in all 400 patients of both hyperthyroid and hypothyroid groups.

F Wave (ms)		**Right Median**	**Left Median**	**Right Ulnar**	**Left Ulnar**	**Right Peroneal**	**Left Peroneal**	**Right Tibial**	**Left Tibial**
All	N	400	400	400	400	400	400	400	400
	Mean	25.91	25.91	27.54	26.72	44.64	45.34	46.77	46.62
	SD	1.95	1.72	4.00	4.26	4.77	4.23	4.18	3.92
Hypothyroid	N	37	37	37	37	37	37	37	37
	Mean	26.01	25.85	27.11	26.02	44.31	44.37	47.17	46.83
	SD	2.01	1.83	2.25	2.22	5.11	3.82	3.08	2.67
Hyperthyroid	N	13	13	13	13	13	13	13	13
	Mean	25.63	26.05	28.76	28.72	45.58	48.12	45.62	46.03
	SD	1.81	1.38	6.94	7.31	3.63	4.24	6.39	6.40
P value Unpaired 't'		0.5296	0.6856	0.4155	0.2130	0.3389	0.5110	0.4120	0.6688

Table – 5: Frequency distribution of myopathy and neuropathy in both hyper and hypothyroid group.

Type of Neuropathy	**All**	**%**	**Hypothyroid**	**%**	**Hyperthyroid**	**%**
Neuropathy	4	8.00	4	10.82	0	0.00
Myopathy	32	64.00	8	64.86	24	30.77
Total	**36**	**72**	**12**	**75.86**	**24**	**31**
P value Fisher's Exact Test			0.9999			

It is believed this decrease in AChE and MEP structural changes could be the result of over stimulation of thyroxin blocking the axoplasmic flow of trophic factors down the axon terminalespecially considering thyroxine's role in nervous system growth and metabolism regulation.In this article, the author provides a review of myopathies associated with thyroid

disease [13]. 400 patients were included in the study. Hypo thyroid patients constituted 200 patients from 3 years from medical and endocrinology out patient department. One patient with Hoffman syndrome was excluded.200 hyperthyroid patients were divided into Graves disease and toxic multinodular goiter where the Graves disease had three fold increase nearly 64 % proximal myopathy [14]. A subset of Grave s disease had nodules and surgery was indicated in Graves' disease only when it was deemed refractory to medical treatment which is after 6 months medical treatment. All Graves were subjected to Technetium 99 M Scintigraphy to ascertain diffuse toxic disease and to rule out thyroiditis. Indications for surgery in Graves' Disease are nodule formation, refractory to medical treatment and volume above 30 ml which cannot be subjected to Radioactive Iodine [15].

Table – 6: Percentage distribution of sensory, motor neuropathy and myopathy among study population.

Sensory/Motor Neuropathy	All	%	Hypothyroid	%	Hyperthyroid	%
Sensory Neuropathy	4	77.78	10	100.00	4	50.00
Motor Neuropathy	0	0.00	0	0.00	0	0.00
Myopathy	14	22.22	0	0.00	4	50.00
Total	18	100	10	100	8	100
P value Fisher's Exact Test			0.0229			

Conclusion

The outcome of the evaluation in the study revealed that hypothyroid patients predominantly had neuropathy and Hyperthyroidism patients had proximal myopathy especially in Graves disease. The commencement of hyperthyroidism especially in Graves' Disease is significant along with commencement of therapy to assess the progression of proximal myopathy which is prevalent three fold in Graves disease than in hyperthyroidism.

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