A NERVE CONDUCTION STUDY IN HYPOTHYROID PATIENTS WITH SYMPTOMATIC Vs ASYMPTOMATIC PERIPHERAL NEUROPATHY IN CORRELATION WITH SERUM VIT B12 LEVEL

Dissertation submitted to

THE TAMILNADU Dr.M.G.R.MEDICAL UNIVERSITY

In partial fulfillment of the regulations

For the award of the degree of

M.D.GENERAL MEDICINE [BRANCH – I]

DEPARTMENT OF GENERAL MEDICINE

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TIRUCHIRAPALLI

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This is to certify that the dissertation entitled **"A NERVE CONDUCTION STUDY IN HYPOTHYROID PATIENTS WITH SYMPTOMATIC Vs ASYMPTOMATIC PERIPHERAL NEUROPATHY IN CORRELATION WITH SERUM VIT B12 LEVEL "** is a bonafide original work of **Dr T.SIVAKUMAR** in partial fulfillment of the requirements of M.D General Medicine [Branch- 1] examination of **THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY** to be held in April 2017.

Prof.Dr.N.K.SENTHILNATHAN .M.D.,
Professor and HOD,
Department of General Medicine,
K.A.P.V Govt. Medical College &
M.G.M.G.H, Tiruchirapalli.

Prof.Dr.D.NEHRU M.D., D.M.R.D.,
Chief, Medicine Unit II,
Department of General Medicine,
K.A.P.V Govt. Medical College &
M.G.M.G.H, Tiruchirapalli.

.

Prof. Dr. S.MARY LILLY M.D.,
DEAN,
K.A.P.V. GOVT.MEDICAL COLLEGE & M.G.M.G.H,
TIRUCHIRAPALLI.

.

DECLARATION

I solemnly declare that the dissertation titled **"A NERVE CONDUCTION STUDY IN HYPOTHYROID PATIENTS WITH SYMPTOMATIC Vs ASYMPTOMATIC PERIPHERAL NEUROPATHY IN CORRELATION WITH SERUM VIT B12 LEVEL"** is done by me at K.A.P.VISWANATHAM GOVT MEDICAL COLLEGE and M.G.M. GOVERNMENT HOSPITAL, TIRUCHIRAPALLI-1 under the guidance and supervision of **Prof. Dr.D.NEHRU M.D., D.M.R.D.,** This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirements for the award of M.D Degree [Branch-1] in General Medicine.

Place: Tiruchirapalli
Date:

Dr.T.SIVAKUMAR
Postgraduate student,
M.D. General Medicine,
K.A.P.V Government Medical college,
M.G.M. Government hospital,
Tiruchirapalli.

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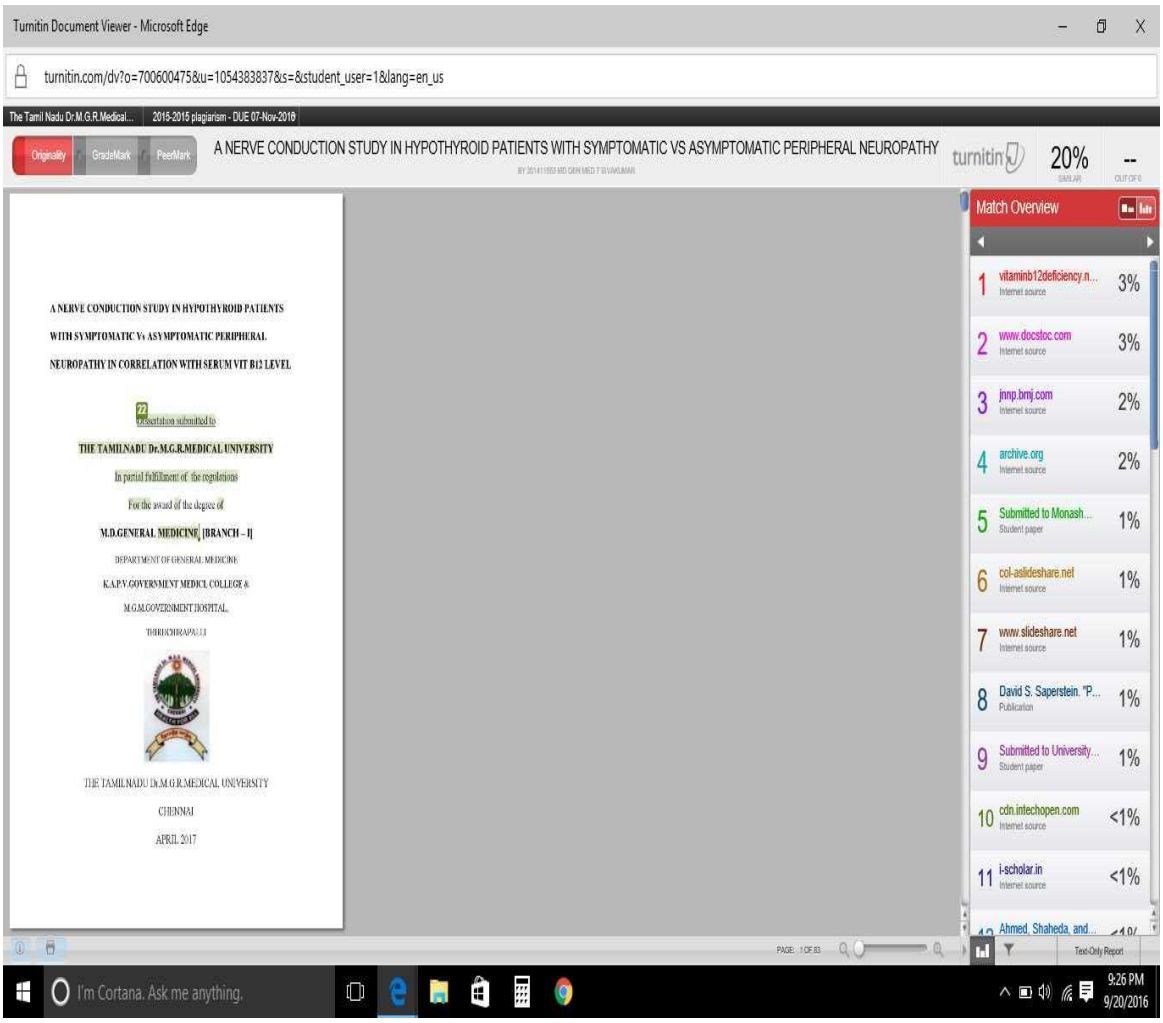
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CONTENTS

ABBREVIATIONS

ACE	:	Angiotensin-converting enzyme
ANA	:	Antineutrophil antibody
ANCA	:	Antineutrophil cytoplasmic antibody
ATD	:	Anti Thyroid drugs
CD	:	Cluster of differentiation
CLIA	:	Clinical Laboratory Improvement Amendments
CMAP	:	Compound nerve action potential
CMT	:	Charcot–Marie–Tooth disease
CTLA 4	:	cytotoxic T-lymphocyte-associated protein 4
DIT	:	Diiodotyrosine
HIV	:	Human immune deficiency virus
HLA	:	Human leukocyte antigen
I^-	:	Inorganic iodide
IFN-γ	:	Interferon γ
MIT	:	Monoiodotyrosine
NAP	:	Nerve action potential
NCS	:	Nerve conduction study
SLE	:	Systemic lupus erythematosis
SNAP	:	Sensory nerve action potential
T3	:	Triiodothyronine

T4	:	Tetra iodothyronin,thyroxine
TBII	:	Thyrotropin-binding inhibitory immunoglobulin
Tg	:	Thyroglobulin
TNF	:	Tumor necrosis factor
TPO	:	Thyroperoxidase
TRH	:	Thyroid releasing hormone
TSH	:	T hyroid stimulating hormone
TSH-R	:	T hyroid stimulating hormone receptor

INTRODUCTION

Hypothyroidism is a common hormonal disorder characterized by a broad clinical spectrum ranging from an asymptomatic or subclinical condition to overt state of myxoedema, end-organ effects and multisystem failure.(1).

The prevalence of hypothyroidism in the developed world is about 4-5% and subclinical hypothyroidism is about 4-15%.(2).

The association of polyneuropathy in hypothyroidism was a well recognized thing even in 1970s. Shirabe et al., did a study and suggested that myxoedema causes metabolic disorder of Schwann cells, resulting in segmental demyelination and turns in to an intrinsic polyneuropathy, not simply compressive neuropathy only due to mucinous deposits in the peripheral nerves (Shirabe et al.,1975) (1).

Peripheral nervous system involvement in hypothyroidism is a well documented fact (3). The study which was done earlier showed prevalence of neuromuscular disorders related to thyroid dysfunction is about 20-80%.The severity of peripheral neuropathy is correlates with the degree and duration of hormonal deficiency or hypothyroidism.(3).

Peripheral nerve abnormalities which are observed in hypothyroidism are entrapment neuropathy or sensory motor

polyneuropathy. Retrospective electrophysiological studies in patients with thyroid disease undergoing treatment are reported.(3).

And in hypothyroid patients there is vitamin B12 deficiency also. It is found that a very elevated prevalence (about 40%) of vitaminB12 in hypothyroid patients. In many cases usual clinical symptoms told by patients are not good indicators of the presence of vitamin B12 deficiency. So that routine testing for vitamin B12 levels may be helpful in hypothyroid patients.(4).

Hence, the objective of the current study is to find out the frequency of peripheral neuropathy in hypothyroidism by conducting nerve conduction study in symptomatic and asymptomatic patients for peripheral neuropathy and to correlate those findings with serum vitamin B12 level among them.

AIMS AND OBJECTIVES

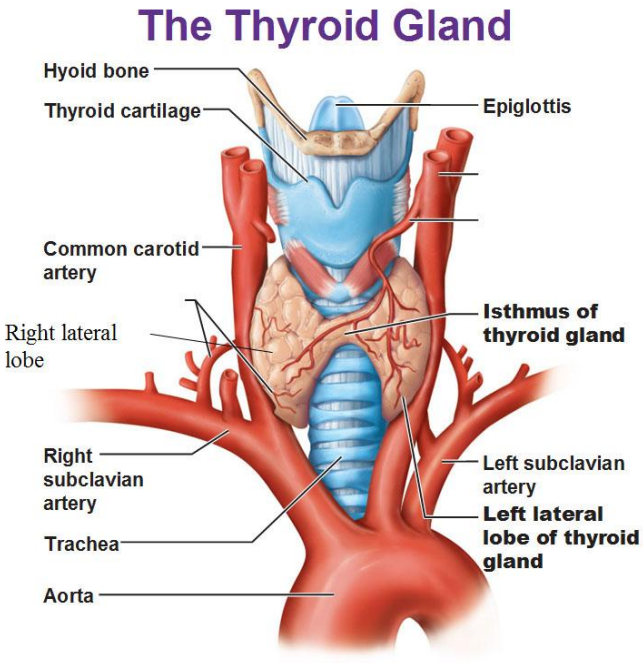
- To study about the frequency of peripheral neuropathy in hypothyroidism patients with symptoms of peripheral neuropathy, by doing nerve conduction study.
- To find out the peripheral neuropathy in hypothyroidism patients who are asymptomatic for peripheral neuropathy, by doing nerve conduction study.
- To find out the correlation of peripheral neuropathy in hypothyroidism patients in relation with serum vitamin B12 levels.

REVIEW OF LITERATURE

Functional anatomy, physiology of Thyroid Gland

Thyroid gland is located in anterior aspect of the neck, with close relation to the first part of the trachea. The thyroid gland in human, has one slender central part, known as isthmus which connects lateral lobe of either side and as a whole which give a "butterfly" shape.

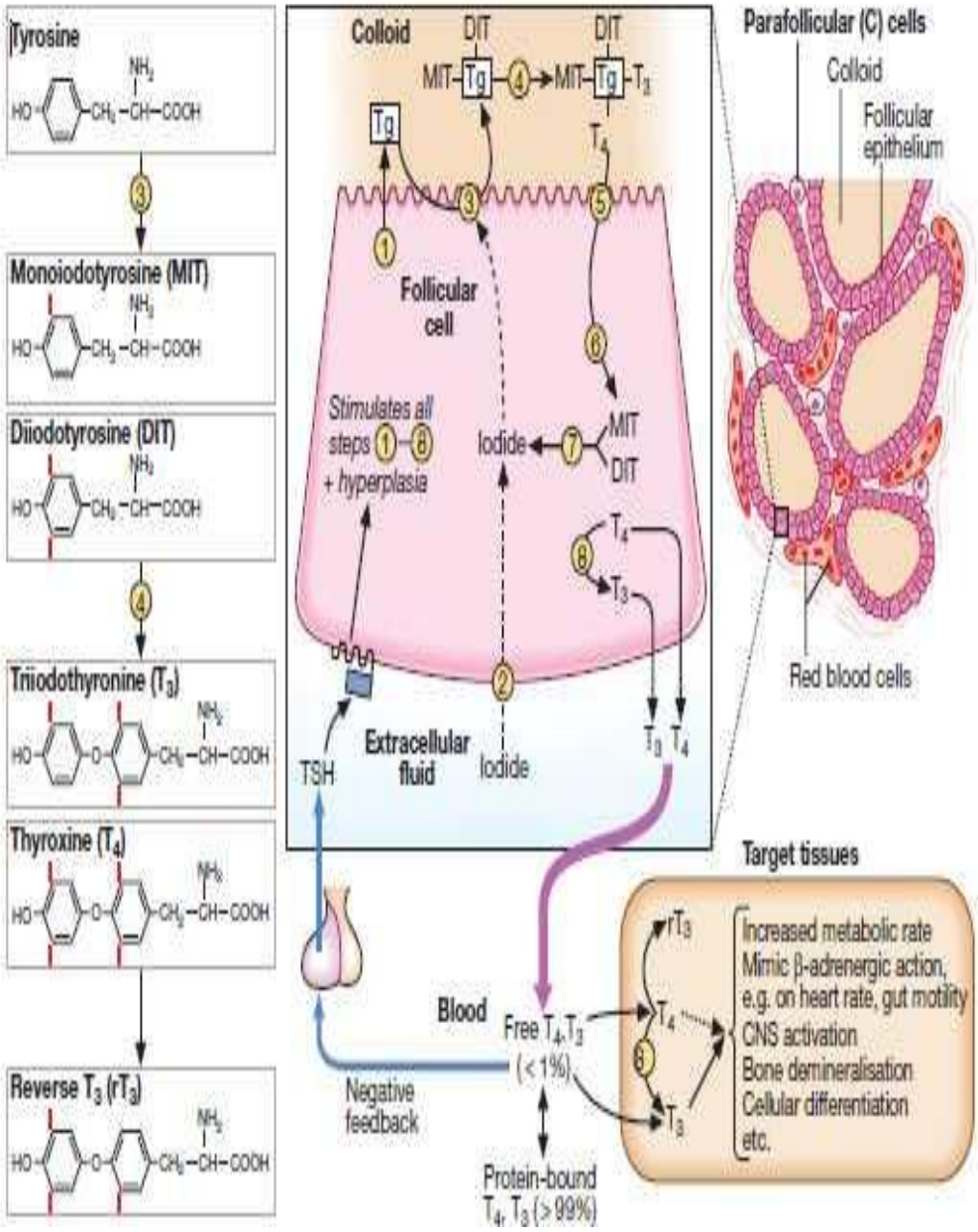
It is one of the biggest of endocrine organs; the thyroid weighs about 15 g to 20 g in adults, with each lobe being approximately 4 cm (height) × 2 cm (width) × 2 cm to 2.5 cm (thickness). The two lobes are connected by the isthmus, which is approximately 2 cm in height and width and 0.5 cm in thickness. It receives blood from the superior and inferior thyroid arteries. Thyroid glands are brownish-red in color.(5)



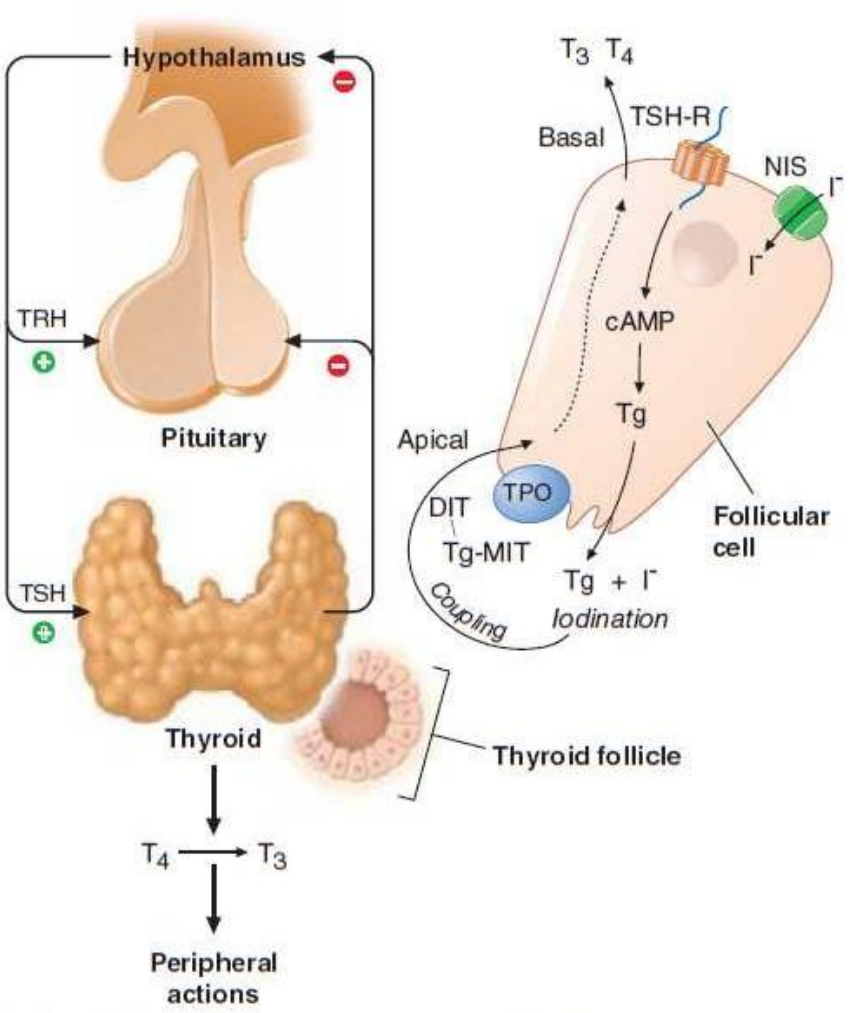
Gross anatomy of the thyroid gland, anterior view

Structure and function of the Thyroid Gland

1. Thyroglobulin (Tg) is synthesized and secreted into the colloid of the follicle.
2. Inorganic iodide (I−) is actively transported into the follicular cell (‘trapping’).
3. Iodide is transported on to the colloidal surface by a transporter (pendrin, defective in Pendred’s syndrome) and ‘organified’ by the thyroid peroxidase enzyme, which incorporates it into the amino acid tyrosine on the surface of Tg to form monoiodotyrosine (MIT) and diiodotyrosine (DIT).
4. Iodinated tyrosines couple to form T3 and T4.
5. Tg is endocytosed.
6. Tg is cleaved by proteolysis to free the iodinated tyrosine and thyroid hormones.
7. Iodinated tyrosine is dehalogenated to recycle the iodide.
8. T4 is converted to T3 by 5′-monodeiodinase.


Tyrosine
Monoiodotyrosine (MIT)
Diiodotyrosine (DIT)
Triiodothyronine (T_3)
Thyroxine (T_4)
Reverse T_3 (rT_3)
Colloid
DIT
MIT
Tg
T_3
T_4
Follicular cell
Stimulates all steps 1–8 + hyperplasia
Iodide
TSH
Extracellular fluid
Parafollicular (C) cells
Follicular epithelium
Red blood cells
Target tissues
Blood
Free T_4, T_3 (< 1%)
Protein-bound T_4, T_3 (> 99%)
Negative feedback
Increased metabolic rate
Mimic β-adrenergic action, e.g. on heart rate, gut motility
CNS activation
Bone demineralisation
Cellular differentiation
etc.

(6)



Regulation of thyroid hormone synthesis. ***Left.*** Thyroid hormones T_4 and T_3 feed back to inhibit hypothalamic production of thyrotropin-releasing hormone (TRH) and pituitary production of thyroid-stimulating hormone (TSH). TSH stimulates thyroid gland production of T_4 and T_3. ***Right.*** Thyroid follicles are formed by thyroid epithelial cells surrounding proteinaceous colloid, which contains thyroglobulin. Follicular cells, which are polarized, synthesize thyroglobulin and carry out thyroid hormone biosynthesis (see text for details). DIT, diiodotyrosine; MIT, monoiodotyrosine; NIS, sodium iodide symporter; Tg, thyroglobulin; TPO, thyroid peroxidase; TSH-R, thyroid-stimulating hormone receptor.

THE THYROID GLAND(7**)**

Hypothyroidism

Hypothyroidism is produced by either anatomical or functional derangement of thyroid gland which may interferes on the process of the making of enough amount of thyroid hormone. Hypothyroidism is a quite frequent condition, and many studies said that the prevalence is 0.3% for overt hypothyroidism and 4% for subclinical hypothyroidism.(8)

Epidemiology

Prevalence

Hypothyroidism due to autoimmune cause is observed up to 4 / 1000 women and 1 / 1000 men as the mean annual incidence rate. It is commonly seen in few populations, just like the Japanese. It is may be, most likely, because of genetics and persistent consumption of foods with more iodine content.

The annual risk is about 4% for developing clinical hypothyroidism if they have positive TPO antibodies (7)

Magnitude of the Problem in India

In sample surveys, covering all the States including Tamilnadu and Union Territories, conducted in 325 districts, it was found that 263 districts where the prevalence of iodine deficiency disorders was >10%

(endemic). It is estimated that >71 million persons suffer from iodine deficiency disorders and goitre. (5).

CAUSES OF HYPOTHYROIDISM

Primary hypothyroidism with goitre

- Acquired

  Iodine deficiency disorders

  Hashimoto's thyroiditis

  ATD treatment

  Goitrogen exposure

- Congenital

  Defects in thyroid hormonogenesis

  Iodide transport or utilization defect

Primary hypothyroidism with atrophic gland

- Acquired

  Atrophic thyroiditis

  Post-ablative hypothyroidism (radioiodineherapy,surgery)

- Congenital

  Thyroid dysplasia

  Thyroid agenesis

Transient primary hypothyroidism

After thyroiditis: silent, subacute or post-partum thyroiditis

CENTRAL HYPOTHYROIDISM

Acquired

Pituitary or hypothalamic disease, e.g., tumor, hemorrhage, granulomatous disease, hypophysitis

Congenital

TSH deficiency or TSH receptor defects

Resistance to thyroid hormone action

Generalised resistance to thyroid hormone action (5)

Pathogenesis

In Hashimoto's thyroiditis, usual findings in thyroid gland are a profound infiltration by lymphocytes, degeneration of the thyroid follicles, formation of germinal center, oxyphil metaplasia, mild to moderate fibrosis and more over absence of colloid.

In atrophic thyroiditis, there is severe fibrosis with less pronounced lymphocyte infiltration. And thyroid follicles are most probably entirely absent.(7)

Atrophic thyroiditis denotes an end phase of Hashimoto's thyroiditis. Environmental as well as genetic factors may increase he susceptibility to autoimmune hypothyroidism.(7).

A weak association is found among autoimmune hypothyroidism and polymorphisms in *CTLA-4*. The relationship is explained as these inherited relations are shared by further autoimmune diseases mainly vitiligo, Addison's disease, pernicious anemia and type 1 diabetes mellitus. (7).

Sex steroid effects on the immune response is most likely cause for the female preponderance of thyroid autoimmunity, further an X chromosome–linked genetic feature is as well possible and in Turner's syndrome the same, possibly, will clarify the high occurrence of autoimmune hypothyroidism. (9)

Ecological vulnerability factors, at present, are inadequately defined. The risk of autoimmune hypothyroidism increases if there is a lofty intake of iodine and low exposure to infections in childhood. These things may account for the raise in prevalence over the 10 to 20 years.(9)

In thyroid, lymphocytic infiltration happens mainly due to activated CD4+ and CD8+ T cells in addition to B cells. And the CD8+ cytotoxic T cells mediate thyroid cell destruction by means of perforin-induced cell necrosis otherwise apoptosis. And cytokines produced by

local T cells such as interferon γ (IFN-γ), Interleukin I , tumor necrosis factor (TNF) may causes thyroid cells very much susceptible for it. These cytokines interfere thyroid functions and trigger additional proinflammatory molecules by the thyroid cells are class I and class II molecules of HLA group, cytokines, adhesion molecules, nitric oxide ,and CD40 (9).

Thyroid autoimmunity is detected by presence of biomarkers such as antibodies to TPO and Tg. In the thyroid gland, complement membrane-attack complexes and complements are fixed by TPO antibodies. (9)

TSH-R antibodies are seen in up to 20% of patients, which never excite the receptor but check the binding of TSH. Therefore, they produce hypothyroidism as well as thyroid atrophy in Asian patients. (9)

Thyrotropin-binding inhibitory immunoglobulin (TBII) estimations which will assess the binding of antibodies to the receptor via antagonism with radiolabeled TSH do not make a distinction between TSI- and TSH-Blocking antibodies; however an affirmative result in a patient with spontaneous hypothyroidism is more proof for the existence of blocking antibodies. (9)

Clinical Manifestations:

The onset is typically insidious, moreover the patient may realize or aware of symptoms only after later stages. But Hashimoto's thyroiditis may present early because of the prominent thyroid swelling sooner than other complaints of existing hypothyroidism.

The thyroid swelling usually is not bulky; however it is more often uneven and firm in consistency. In many cases pyramidal lobe is palpable, which is in general a residue of the thyroglossal duct. Seldom, Hashimoto's thyroiditis without complications will present with pain.(10)

Otherwise, patients with atrophic thyroiditis or late stage of Hashimoto's thyroiditis present with may come with symptoms features of hypothyroidism. The skin becomes thin and dry as well as seen with decreased sweating. Skin thickening without pitting (*myxoedema*) is due to water traps by increased dermal glycosaminoglycan content and this gives the distinctive features consist of a puffy face with edema of eyelids in addition to pretibial edema of nonpitting type .(10)

There is carotene accumulation frequently which gives a yellowish tinge to the skin. Nail growth rate is reduced. Hair becomes dry, frail, and not easy to handle so that falls away easily. There is reduction of the lateral 1/3 rd of the eyebrow and diffuse alopecia(10)

Other frequent features consist of constipation and weight gain (in spite of a poor desire for food). The weight increase is usually modest which primarily caused by retention fluid by myxoedema.

In both sexes libido is in low level; and in females many patients have amenorrhea otherwise oligomenorrhea in chronic cases, but menorrhagia is also frequently seen. The incidence of miscarriage is increased and fertility is reduced.(10).

There will be a reduced stroke volume and bradycardia due to reduced myocardial contractility and pulse rate. Increased peripheral resistance may cause hypertension, particularly diastolic. Patient may feel cool extremities due to diversion of blood from the skin. Pericardial effusions is seen in nearly 30% of cases but may not reduce cardiac function . Even though changes in expression of myosin heavy chain isoform is documented, cardiomyopathy is not usually seen. Accumulation of fluid in other serous cavities are seen such as in the middle ear compartment, causes reduced hearing due to defective conduction. (10)

Respiratory functions are usually not abnormal. In some cases dyspnea may be due to sleep apnea, impaired respiratory muscle function, pleural effusion, and diminished ventilatory drive.

Entrapment syndromes such as carpal tunnel syndrome are frequently seen, as is defective muscle function with pain, stiffness, and cramps.

Clinically, we can find pseudomyotonia, slowness in tendon reflexes relaxation . There may be impairment of memory and concentration.(10)

Uncommon neurologic conditions include myxoedema coma, reversible cerebellar ataxia, psychosis and dementia.

Hashimoto's encephalopathy is a syndrome with TPO antibodies , clinically with myoclonus, and evidences of slow-wave activity on electroencephalography which respond to steroid therapy , at the same time the association with autoimmunity of thyroid gland or hypothyroidism is not well recognized.

Fluid accumulation in vocal cords as well as in tongue manifest as hoarseness of voice and occasionally clumsy speech. (10).

Clinical findings of Hypothyroidism:

Symptoms

- Feeling coldness
- Dryness of skin
- Tiredness, weakness
- Memory impairment
- Problems in concentration
- Hair loss
- Constipation
- Weight gain instead of of poor appetite
- Shortness of breathing
- Hoarseness of voice
- Paresthesia
- Menorrhagia (later oligomenorrhea or amenorrhea)
- Hard of hearing

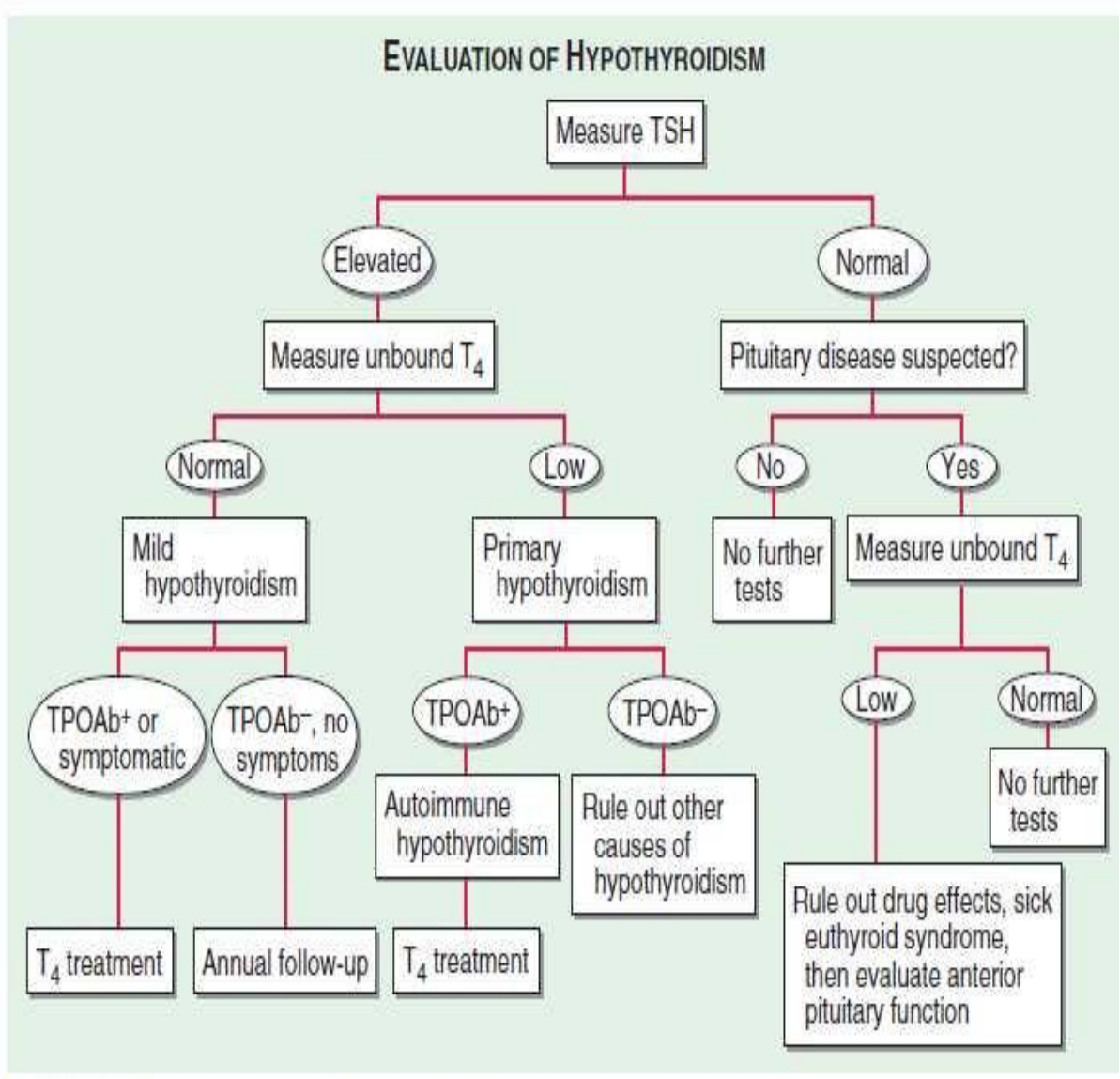
Signs

- Puffyness of face and hands as well as feet (myxedema)
- Diffuse alopecia
- Dry coarse skin; cool peripheral extremities
- Bradycardia

- Peripheral edema
- Carpal tunnel syndrome
- Delayed relaxation of tendon reflex
- Effusions of Serous cavity (10)

Laboratory Evaluation:

A synopsis of the laboratory tests used to diagnose the presence and cause of hypothyroidism is listed below.



Evaluation of hypothyroidism. TPOAb+, thyroid peroxidase antibodies present; TPOAb−, thyroid peroxidase antibodies not present; TSH, thyroid-stimulating hormone.

(7)

A normal range of TSH level usually excludes primary hypothyroidism (and not secondary one) which may be used as a screening test . In case of TSH is elevated, to validate the occurrence of clinical hypothyroidism, an unbound T4 level is needed but it will not identify subclinical hypothyroidism. Approximately, in 25% of patients circulating unbound T3 levels are normal which is reflecting adaptive deiodinase responses to hypothyroidism. So that usually T3 study is not required.

After clinical otherwise subclinical hypothyroidism is established, the cause is generally labeled after finding the positivity of TPO antibodies, which are usually seen in >90% cases of hypothyroidism of autoimmune problems. TBII may be detected in 10–20% of cases, but measurement is seldom recommended. Biopsy by FNA may be done to prove the existence of autoimmune thyroiditis.

Other useful abnormal biochemical test results in hypothyroidism may possibly include elevated triglycerides, cholesterol in addition to increased creatine phosphokinase. There will be anemia, generally of normocytic or macrocytic type. If there is no coexistence of iron deficiency, the anemia and additional abnormalities slowly resolve with thyroxine replacement therapy.(10)

Treatment of Hypothyroidism

Clinical Hypothyroidism

The usual daily replacement dose of levothyroxine is 1.6 μg / kg body weight (in most cases 100 – 150 μg), if there is no residual function of thyroid. It should be preferably taken 30 minutes prior to breakfast. For most of the patients lower doses may be sufficient until remaining thyroid tissue is damaged. Adult patients under 60 years who are not a known case of cardiac illness may possibly be started on 50–100 μg levothyroxine (T4) daily.

This dose adjustment is made on the basis of TSH estimations, with the aim of therapy to maintain the lower half of the normal TSH levels. TSH responses are gradual. TSH level may be estimated after two months of initiation of management or followed by any next modification in levothyroxine dosage.

Clinically, the effects of levothyroxine substitution therapy appear slowly. Patients may feel full relief from symptoms after three to six months when normal TSH levels are regained. If the TSH is high, modification of dosage of levothyroxine is to be done in 12.5- or 25-μg increments and decrements of the same range to be done if the TSH is low. Patients living with a low TSH level of any basis have an increased risk for reduced bone density and atrial fibrillation.

Monitoring of TSH level is done every once in 12 months intervals and or every two to three years in case a normal TSH is maintained for some years.

Patients may discontinue treatment as they don’t find any difference in symptoms if they miss few doses .So that it is important to ensure ongoing adherence. As T4 has a long half-life (7 days), if a patient forget a dose can take the skipped tablets at once. (11)

Subclinical Hypothyroidism

Subclinical hypothyroidism refers to biochemical evidence of thyroid hormone deficiency in patients who have few or no universally accepted recommendations for the management of subclinical hypothyroidism, but levothyroxine is recommended if the patient is a woman who wishes to conceive or is pregnant, or when TSH levels are above 10 mIU/L. When TSH levels are below 10 mIU/L, treatment should be considered when patients have symptoms suggestive of hypothyroidism, positive TPO antibodies, or any proof of heart disease. After monitoring about 3 months treatment is started if TSH is elevated. Treatment is started with a low dose of levothyroxine (25–50 μg/d) to bring TSH level to normal. If levothyroxine is not given, thyroid function to be done annually.(11)

PERIPHERAL NEUROPATHIES

Disorders of the peripheral nervous system are common and may affect the motor, sensory or autonomic components, either in isolation or combination. The site of pathology may be nerve root (radiculopathy), nerve plexus (plexopathy) or nerve (neuropathy). Neuropathies may present as mononeuropathy, multiple mononeuropathies or a symmetrical polyneuropathy. (12)

Pathophysiology

Damage which may occur to the nerve cell body (axon) or the myelin sheath (Schwann cell), leading to axonal or demyelinating neuropathies. The distinction is important, as only demyelinating neuropathies are usually responding to treatment; making the distinction requires neurophysiology (nerve conduction studies and electromyography, Neuropathies can occur in association with many systemic diseases, toxins and drugs.(12)

Causes of polyneuropathy

Genetic

- Charcot–Marie–Tooth disease (CMT)
- Hereditary neuropathy with liability to pressure palsies (HNPP)

  Familial amyloid polyneuropathy
- Hereditary sensory autonomic neuropathies (HSN, HSAN)

- Hereditary neuralgic amyotrophy

Drugs

- Antiretroviral
- Antibiotics (dapsone, isoniazid, metronidazole, ethambutol)
- Amiodarone
- Phonation
- Chemotherapy (cisplatin, vincristine, thalidomide)

Toxins

- Nitrous oxide (recreational use)
- Alcohol
- Rarely: lead, arsenic, mercury, organophosphates, solvents

Vitamin deficiencies

- Pyridoxine
- Thiamin
- Vitamin B12
- Vitamin E

Infections

- Leprosy
- HIV
- Brucellosis

Inflammatory

- Chronic inflammatory demyelinating polyradiculoneuropathy
- Guillain–Barré syndrome
- Paraneoplastic (antibody-mediated)

Vasculitis (polyarteritis nodosa, granulomatosis with polyangiitis (also known as Wegener's granulomatosis), rheumatoid arthritis, SLE)

Systemic medical conditions

- Diabetes
- Sarcoidosis
- Renal failure

Malignant disease

- Infiltration

Others

- Amyloidosis
- Paraproteinaemias
- Critical illness polyneuropathy/myopathy

Common causes of axonal and demyelinating chronic polyneuropathies

Axonal

- Cirrhosis
- Alcohol
- Diabetes mellitus
- Uraemia
- Myxoedema
- Acromegaly
- Amyloid
- Paraneoplastic
- Drugs and toxins
- Deficiency states
- Hereditary
- Infection
- Idiopathic

Demyelinating

- Multifocal motor neuropathy
- Chronic inflammatory demyelinating polyradiculoneuropathy
- Charcot – Marie – Tooth disease type I and type X
- Paraprotein-associated demyelinating neuropathy

Clinical features

If motor nerve is involved there will be features of a lower motor neuron type of lesion. Clinical features of sensory nerve participation depend on the kind of sensory nerve involved; small-fiber neuropathies are often painful. Autonomic involvement may cause postural hypotension, disturbance of cardiac rhythm, sweating, and bladder and sexual functions and gastrointestinal functions; rarely isolated autonomic neuropathies are there, and more commonly complicate other neuropathies.

Initial tests

- Glucose (fasting)
- C-reactive protein
- Full blood count
- Erythrocyte sedimentation rate,
- Liver function tests
- Urea and electrolytes
- Vitamin B12, folate
- Serum protein electrophoresis
- ANA, ANCA
- Chest X-ray• HIV testing

(13)

If initial tests are negative

- Nerve conduction studies
- Vitamins E and A
- Serum amyloid
- Lyme serology
- Genetic testing
- Serum ACE

(ACE = angiotensin-converting enzyme; ANCA = antineutrophil cytoplasmic antibody; ANA = antineutrophil antibody)

Entrapment neuropathy

Focal compression or entrapment of nerve is the common cause of a mononeuropathy. Symptoms and signs of entrapment neuropathy are listed here. Entrapment neuropathies may affect anyone, but diabetes, excess alcohol or toxins, or genetic syndromes may be predisposing causes. Entrapment neuropathies will usually recover, unless axonal loss has occurred, provided the primary cause is removed, either by avoiding the precipitation of activity or by surgical decompression.(14)

Muscle weakness/ muscle-wasting And Area of sensory loss :
Median nerve: (at wrist)

The usual symptoms are ache and paraesthesia on palmar aspect of hands and fingers which causes sleep disturbances . Pain may be felt in

arm and shoulder .Lateral part of palm and thumb,index, middle and lateral half 4th finger.

Ulnar: (at elbow)

Paraesthesia is felt on medial border of hand, wasting as well hand muscles weakness . All small muscles of hand, excluding abductor pollicis brevis Medial palm and little finger, and medial half 4th finger

Radial Weakness of extension of wrist and fingers, often precipitated by sleeping in abnormal posture, e.g. arm over back of chair Wrist and finger extensors, supinator, dorsum of thumb.

Common peroneal Foot drop, trauma to head of fibula Dorsiflexion and eversion of foot or dorsum of foot

Lateral cutaneous nerve of the thigh (meralgia paraesthetica)

Tingling and dysaesthesia on lateral border of thigh (14)

Polyneuropathy

A polyneuropathy is usually associated with a 'length dependent' pattern, which occurs first in the longest peripheral nerves of lower limbs before the upper limbs. Sensory symptoms and signs develop in an ascending 'glove and stocking' distribution

In inflammatory demyelinating neuropathies, the pathology may be more patchy, affecting the upper rather than lower limbs. (14)

Hypothyroidism

Hypothyroidism is generally associated with a proximal myopathy, however some patients develop a neuropathy, most typically CTS. Infrequently, a generalized sensory polyneuropathy characterized by numbness as well as painful paresthesias in both the legs and hands can occur. These are responds to throxine replacement. (15)

Nutritional Neuropathies Cobalamin (Vitamin B12)

Pernicious anemia is the most common cause of cobalamin deficiency. Other causes include dietary avoidance (vegetarians), inflammatory bowel disease, pancreatic insufficiency, gastrectomy, gastric bypass surgery, bacterial overgrowth, and possibly histamine-2 blockers and proton pump inhibitors.

An underappreciated cause of cobalamin deficiency is food-cobalamin malabsorption. This typically occurs in older individuals and results from an inability to adequately absorb cobalamin in food protein. No apparent cause of deficiency is identified in a significant number of patients with cobalamin deficiency. The use of nitrous oxide as an anesthetic agent or as a recreational drug can produce acute cobalamin deficiency neuropathy and subacute combined degeneration.(15)

Complaints of numb hands characteristically appear earlier than lower extremity paresthesias are noted. A preferential large-fiber sensory

loss causing defective proprioception and vibration with sparing of small-fiber modalities is present; an unsteady gait reflects sensory ataxia. These features, coupled with diffuse hyper reflexia and absent Achilles reflexes, should always focus attention on the possibility of cobalamin deficiency.

Optic atrophy and, in severe cases, behavioral changes ranging from mild irritability and forgetfulness to severe dementia and frank psychosis may appear. The full clinical picture of subacute combined degeneration is uncommon.

CNS manifestations, especially pyramidal tract signs, may be missing, and in fact some patients may only exhibit symptoms of peripheral neuropathy. Diagnostics shows an axonal sensorimotor neuropathy. CNS involvement produces abnormal somatosensory and visual evoked potential latencies.(16)

The diagnosis is made by finding reduced serum cobalamin levels. In up to 40% of patients, anemia and macrocytosis are lacking. Serum methylmalonic acid and homocysteine, the metabolites that accumulate when cobalamin-dependent reactions are blocked, are elevated. Antibodies to intrinsic factor are present in approximately 60%, and antiparietal cell antibodies in about 90%, of individuals with pernicious anemia.

Cobalamin deficiency can be treated usually a typical regimen consists of 1000 μg cyanocobalamin IM weekly for 1 month and monthly thereafter.

Patients with malabsorption for food cobalamin can absorb free cobalamin and therefore can be treated with oral cobalamin supplementation. An oral cobalamin dose of 1000 μg per day is sufficient. Treatment for cobalamin deficiency generally does not completely reverse the clinical manifestations, and at least 50% of patients exhibit some permanent neurologic deficit.(16).

Hypothyroidism and vitamin b12 deficiency

Several complaints of vitamin B12 deficiency are identical to the symptoms of hypothyroidism. Thus, weakness, fatigue, irritability, memory loss, depression, decreased libido, menstrual disturbances and poor mental growth are similar. Prevalence of vitamin B12 deficiency is high in hypothyroidism(approx 40%) is may be Confounding the situation. So that usual symptoms may not be helpful to find out deficiency state of vitamin b12. (4) Looking for serum vitamin B12 levels may be done in every hypothyroid case.(4)

Why hypothyroidism leads to vitamin B_{12} deficiency

Normal cycling of folate results in the formation of an irreversible reaction in which 5, 10 methylenetetrahydrofolate is converted to 5ethyltetrahydrydrofolate (5-MTHF) by the enzyme 5,10 methyltetrahydrofolate reductase (MTHFR). Of note in this reaction is that MTHFR uses FAD (derived from **riboflavin**, vitamin B2) as an essential cofactor.

In addition, the reduction that occurs requires input from NADH + H^+(derived from **nicotinamide**, vitamin B3). In the absence of these two vitamins (B2/B3) the enzyme is not functional. In this situation, folate is not able to recycle via the conversion of 5,10-methenyltetrahydrofolate to 5-methyltetrahydrofolate. This leads to an intracellular deficiency of folate, MeCbl, methionine and SAM.

Synthesis of Flavin Mononucleotide (FMN) from riboflavin requires the addition of phosphate from ATP, via riboflavin kinase, with the input of triiodothryonine (T3) and thyroxine (T4). The subsequent synthesis of FAD from FMN also involves contribution of thyroxin in the presence of FAD plus AMP. If there is reduced level of thyroxine in hypothyroidism that might cause reduced levels of FAD in tissues. In the same way low content of iodine and/or riboflavin may cause reduction in FAD level.

Role of the Thyroid in FAD synthesis

In persons with hypothyroidism, or vitamin B2, or vitamin B3 deficiency, or those who have mutations in the MTHFR gene, the MTHFR enzyme has reduced activity and so the amount of 5MTHF that is synthesized is reduced, and so the 5MTHF + OHCbl <=> THF + MeCbl reaction cannot operate efficiently and hence supplies of MeCbl are rapidly turned into inactive OHCbl. As a result, the typical addition of the methyl group from the folate cycle is decreased and so must be supplied by MeCbl. As the methyl group cannot be recycled via the normal route, every methyl group used in synthesis must be supplied by **MeCbl.** This leads to rapid depletion of Vit B12 stores which may leeds to reduced vitamin b12 levels in hypothyroidism.

Nerve Conduction study

Peripheral nervous system (PNS) functions are studied and recorded by nerve conduction study which will give us:

- Identification of conditions
- Explanation of condition (previous/ fresh ; active/stationary course)

Prospective follow up of illness through various analysis suggests that prediction of disease course and treatment out come could be done on the basis of results and pathology found by NCS.(17)

The Principals of Nerve Conduction Studies

Over the skin of a peripheral nerve an electrical pulse is given to depolarize it which may produce the followings :

1. A forward action potential of the nerve(NAP) which will be marked at a far-away spot on that particular nerve.
2. The activation of muscle fibres in a target muscle supplied by the nerve will gives a compound muscle action potential (CMAP) arising from it. This action potential received and marked by either needle or surface electrodes. Surface electrodes provides data about the conduction time utilized by fastest axons to conduct an impulse which supply that muscle and amount of response.

Surface stimulators are used to stimulate a nerve by placing it over the skin close to nerve root or nerve. Transcutaneous magnetic stimulation are used for a cerebral cortex and spinal root stimulation. Therefore the complete distance end to end of the motor conduit could be assessed.

Techniques of Specific Nerve Conduction Study

Nerve conduction studies of motor fibres:

The recording electrodes are fixed by using adhesive and conductive pads over the skin which covers the particular muscle to be studied. One electrode which is electrically active is placed over the belly of that muscle and inactive electrode is placed over the same muscle tendon. So as to provide a zero voltage reference point, a ground electrode is also fixed some where along the stimulation pathway.

Individual muscle fibre voltage responses are collectively represented by the compound muscle action potential. An initial upward deflection followed by a smaller downward deflection is denotes the shortest latency of the CMAP which is the time from stimulus artifact to onset of the response . The amplitude of CMAP is calculated a point commencing at baseline to peak of negative deflection. (Conventionally in neuroelectrophsiology an upward deflection denotes a negative voltage response.) It is usually recorded in millivolts (mV) .

To record the CMAP, the excitatory current is steadily augmented till a point is achieved which will not give any more gain in the height of the CMAP amplitude. This supramaximal point only gives accurate and reproducible values of amplitude and latency of NCS.

After this a particular nerve is stimulated at a more proximal site for example , in case of median nerve study a point closer to biceps tendon over the antecubital fossa is selected. In physiological conditions if medial nerve is stimulated at the wrist and the elbow gives two similar CMAP of identical shape and amplitude due to innervations of muscles by same nerve.

On the other hand, the latency will vary for a stimulus which is made at elbow and wrist which means the longer distance gives greater latency.

As all other factors involving neuromuscular transmission and muscle activation are common to both stimulation sites, the difference in latency represents the time taken for the fastest nerve fibres to conduct between the two stimulation points. The fastest motor nerve conduction velocity can be calculated by measuring the distance between the two sites as follows: FMNCV (m/s) = distance between stimulation site 1 and site 2 (mm)/[latency site 2 – latency site 1 (ms)].

Conduction Studies of Sensory Fibres:

The recording of nerve action potentials of sensory fibres are obtained by electrically stimulating them and recording the nerve action potential at a The sensory nerve action potential (SNAP) is obtained by electrically stimulating sensory fibres and recording the nerve action potential at a point far away site all along that nerve. Here also a supramaximal stimuli is given. Antidromic nerve conduction study for sensory nerve is done by placing stimuli in a proximal site and recording the effects more distally which is in opposite direction for physiological sensory nerve conductions. On the other hand orthodromic SNAP refers the reversal of the above said method which is in normal physiological sensory nerve conduction mode.

An orthodromic median sensory study is shown in figure .

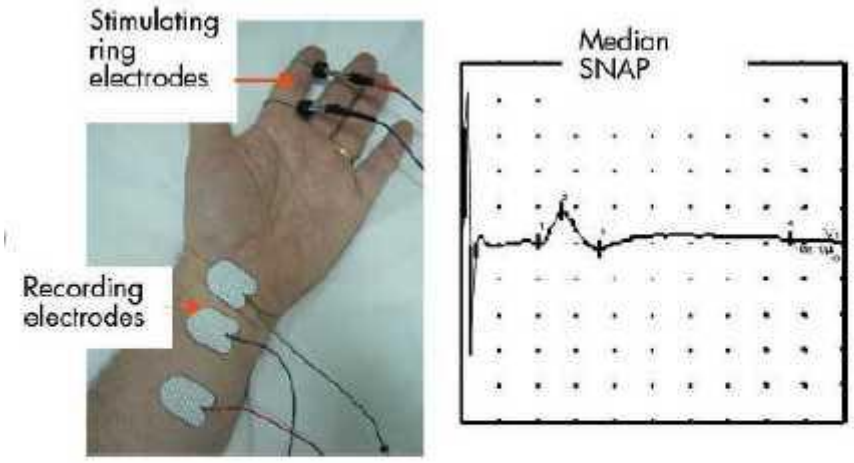


Figure 2 Median orthodromic sensory study. The index finger digital nerves are stimulated via ring electrodes and the response recorded over the median nerve at the wrist.

In SNAP the peak to peak amplitude of potentials and latency will be calculated. As the sensory latency directly correlates the velocity this result could be stated as velocity or a latency over standard distance.

In SNAP about 20% of the fibres which are having fast conducting capacity and largest diameter only studied and they carry the sensations of vibration, fine touch and position sense. In case of predominant small fibre peripheral neuropathy which conduct the pain sensation and represent 80% of fibres, they could not be studied by usual NCS so that results possibly appear as normal.

F Waves:

These are a type of late motor response ,further they are called after as they are first described in foot. From the initial stimulation site an action potential is spread on either side of a motor nerve axon. The CMAP is produced by an impulse which is propagated distally. At the same time an impulse gose on proximal part to the anterior horn cell and makes the axon to back fire via depolarizing the axon hillock. This will lead to a little supplementary muscle depolarization and produce F wave, at a later time. As few, that is around 2% of axons back fire with each stimuli as well as many group of neurons are back fire with each stimulus, F waves may differ in shape and latency. The most reliable measure of the F wave is the minimum latency of 10–20 firings.

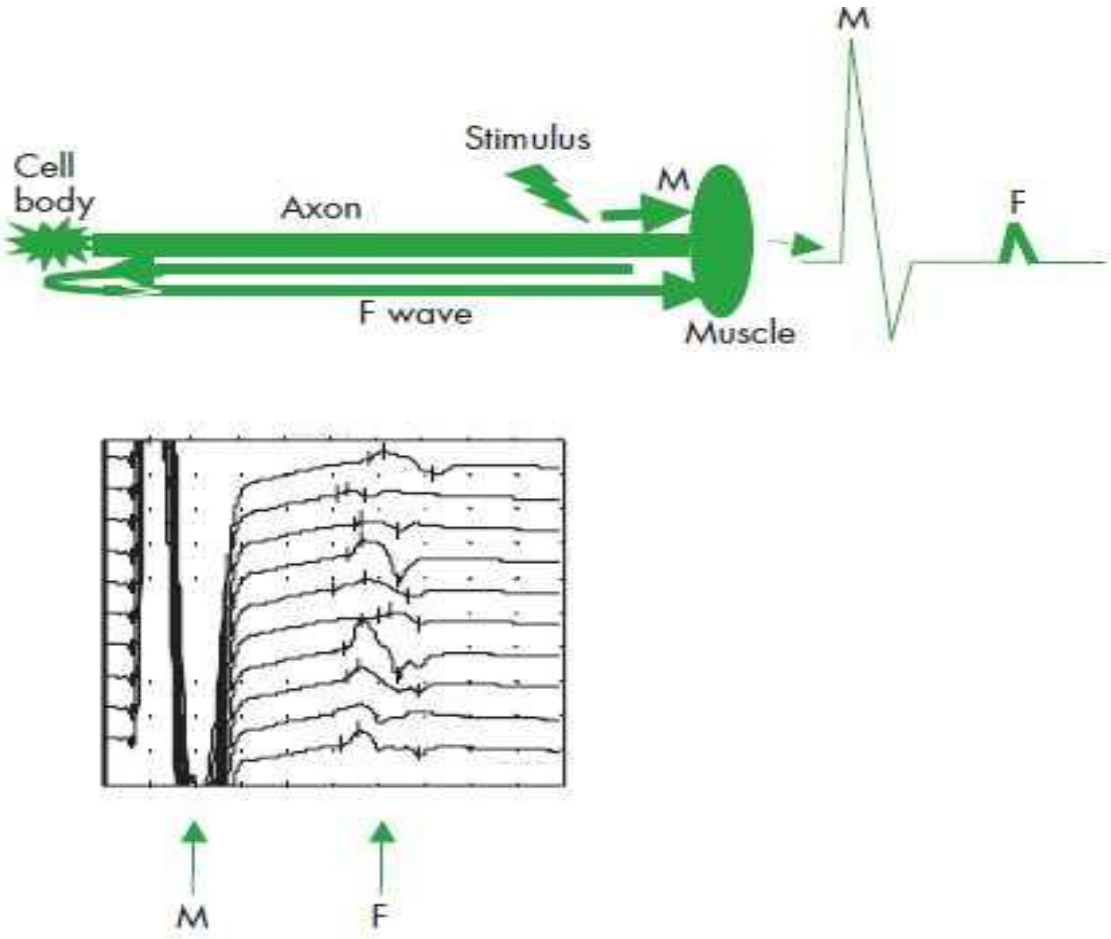


Figure 3 Schematic representation of the early M response from the distally propagated action potential and the later F wave from the proximally propagated action potential. The latter depolarises the axon hillock causing it to backfire. Actual F wave responses are shown in the lower trace. F waves vary in latency and shape due to different populations of axons backfiring each time.

Nerve Conduction Studies in Disease:

General

By analyzing the data of NCS we can get clues about pathophysiological pattern and site of involvement. In general, peripheral neuropathy largely affects myelin or axons. In reality, even though both types of pattern occur in same person usually one pathology predominates.

Table 1 Typical nerve conduction study abnormalities seen with axon loss or demyelination

	Axon loss	Demyelination
Sensory responses	Small or absent	Small or absent
Distal motor latency	Normal or slightly prolonged	Prolonged
CMAP amplitude	Small	Normal (reduced if conduction block or temporal dispersion)
Conduction block/temporal dispersion	Not present (responses may disperse slightly)	Present
Motor conduction velocity	Normal or slightly reduced	Notably reduced
F waves minimum latency	Normal or slightly prolonged	Significantly prolonged

It is not necessary to have all the features of axon loss or demyelination to come to a conclusion. Some conditions only affect motor or sensory nerves, and some processes are length dependent and others universal. It can sometimes be quite difficult to decide whether a process is primarily demyelinating or demyelinating with secondary axonal changes as features of both may coexist.

The outcome of focal lesions depends on the type of the pathological changes found in a particular site. For example , a patient with wrist drop which may be due to radial nerve injury at the spiral groove is more likely recover completely and somewhat earlier 1 ½ to 3 months because of the most probable pathology is focal demyelination. If a lesion is due to significant axonal injury the recovery time will be longer up to 6 months to one year.

So that it is very important to come to a conclusion about the type of the peripheral neuropathy going on in a patient, whether axonal or demyelinating which will be useful to order more investigations and treat one properly.

For example, acute inflammatory demyelinating polyneuropathy the treatment modality is plasma exchange and human immunoglobulin in which the pathology could be segmental demyelination of nerve.

Conversely a length dependent axonal neuropathy developing in a patient on chemotherapy requires reassessment of the chemotherapy or addition of a protective agent. Neuropathies may be classified pathologically in this fashion, anatomically or electro physiologically.

Motor NCS in Axonal Loss

In these conditions, very few axons which in good functional state are connected with muscle fibres .And myelin is not affected. So that the amplitude of CMAP is typically reduced in spite of normal range of latency and velocity. But in longstanding and severe motor axonal neuropathy few of the largest and fastest conducting fibres will be lost. Because of these changes distal motor latency sometimes increased and the conduction velocity to a lesser extent reduced.

Further, the types of pathology manifestations are depend on timings and dynamics of axonal insult. In traumatic complete transaction of nerve, as there is no sufficient time, there are no abnormality seen because of there is no axonal neuropathy developed. The CMAP amplitude will only start to fall a few days later. In generalized

neuropathy there is sluggish loss of axons at the same time left over axons uses the interval to get collateral connections with muscle fibres which will produce normal range of amplitude. Conversely regenerating new fibres shows lesser velocities and extra dispersed CMAP.

In Demyelination

In demyelination the deciding factors of the pathological events are extent and the site of involvement of a nerve. Geneally loss in myelin thickness leads to slowness of conduction; in later stages conduction block leads to saltatory conduction failure. So that NCS records reveal more prolonged motor latencies and markedly reduced conduction velocities. In case of proximal demyelination only findings are F wave abnormalities and the conduction velocity and distal motor latency are seen in a normal range. Conduction block or temporal dispersion both result in a reduction in CMAP amplitude.

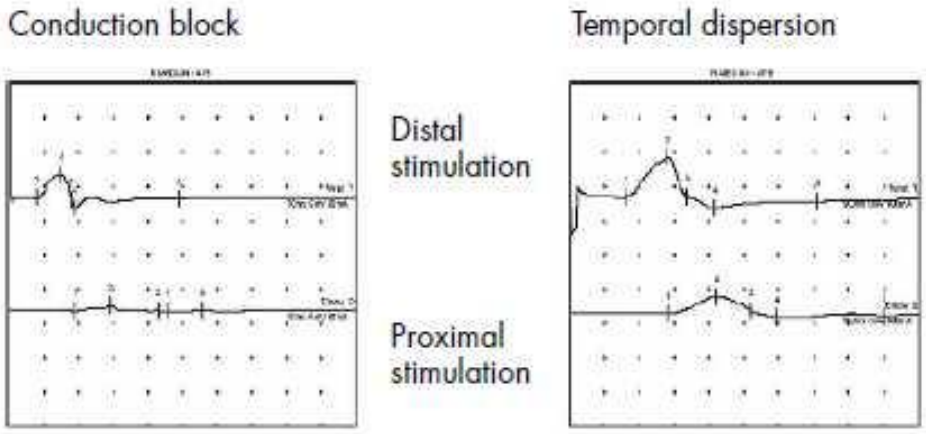


Figure 4 Both these traces show demyelination in median motor studies. The trace on the left shows almost complete conduction block with an absent response with proximal stimulation. The trace on the right shows temporal dispersion where the CMAP duration increases by almost 40% with proximal stimulation. In both situations the CMAP amplitude with proximal stimulation is smaller.

The proximal CMAP duration must not increase by 20% in true conduction blocks. In temporal dispersion there is a loss of synchrony in the nerve action potentials resulting in a loss of CMAP amplitude because the positive part of one muscle fibre action potential cancels out the negative part of another (phase cancellation).

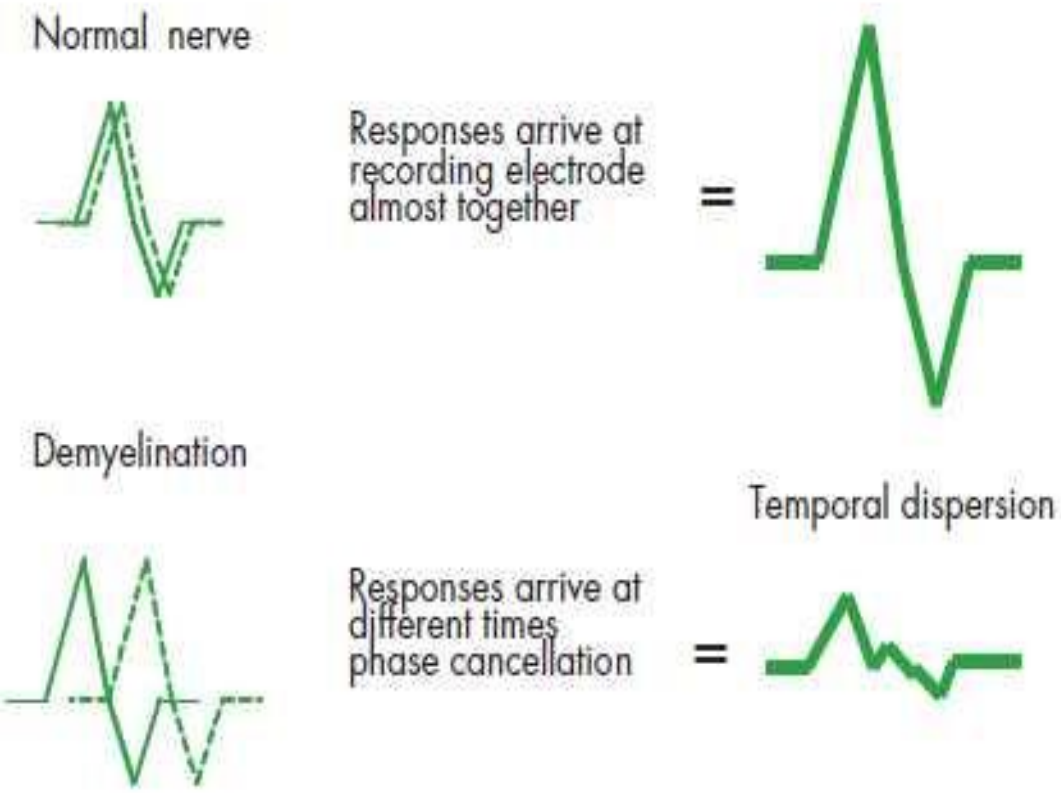


Figure 5 Schematic representation of phase cancellation and temporal dispersion in demyelination. In the normal nerve, the responses are synchronised in time and therefore summate (amplitude is higher that that of the individual components). Temporal dispersion results in an increased duration and reduced amplitude of CMAP.

REVIEW OF PREVIOUS STUDIES

Hande Turker et al done a study titled as Neurological Complications of Hypothyroidism in which they stated that

“In a case study by Shirabe et al., it was suggested that myxoedematous polyneuropathy might be intrinsic neuropathy due to metabolic disorder of Schwann cells related to hypothyroidism, resulting in segmental demyelination, not merely compressive neuropathy due to mucinous deposits in the peripheral nerves (Shirabe et al.,1975). More case studies followed in 80s also (Martin et al., 1983). In a study performed by Magri et al., intraepidermal nerve fiber density reduction was evaluated as a marker of preclinical asymptomatic small-fiber sensory neuropathy in hypothyroid patients. Their findings suggested that a considerable number of untreated hypothyroid patients may have preclinical asymptomatic small-fiber sensory neuropathy (Magri et al., 2010) ” (1)

Dr. A. A Asia et al have done a study Nerve conduction studies in recently diagnosed untreated hypothyroid patients and says “Neuromuscular symptoms were commonly encountered. There was a predominant involvement of sensory nerves, especially the sural nerve and median nerve on nerve conduction study. Early detection can prevent structural alterations in peripheral nerves as they occur later in the

course of the disease and help in initiating replacement therapy at the earliest. 75% patients had distally located paresthesias, 55% complained of cramps and 15% had weakness of the lower limbs .In 19 % subjects both motor and sensory nerves were involved, while in 69 % there was involvement of only sensory nerves. There was slowing of nerve conduction velocity in 71 % patients characteristically for median and sural sensory nerves. Carpal tunnel syndrome was seen in 15% patients."(3)

Jabbar A et al has done a study on vitamin b12 of hypothyroid patients and stated "Many of the symptoms of hypothyroidism are similar to the symptoms of vitamin B12 deficiency. Thus, fatigue, weakness, depression, irritability, memory loss, abnormal menstrual cycles, decreased libido and poor mental growth are similar. to both conditions. Confounding the situation is that there is a high (approx 40%) prevalence of vitamin B12 deficiency in hypothyroid patients. Traditional symptoms are not a good guide to determining presence of B12 deficiency. Screening for vitamin B12 levels should be undertaken in all hypothyroid patients, irrespective of their thyroid antibody status."(4)

MATERIALSAND METHODS

Source of Data:

This study was done at Mahatma Gandhi Memorial Government Hospital attached with K.A.P.V.Govt.Medical college, Thiruchirapalli in collaboration with Department of Biochemistry and Neurology.

Study Design:

Unicentric, crosssectional and analytical study

Period of Study:

1 year from July 2015 to June 2016

Ethics Committee Approval:

Approval and clearance were obtained from the institutional ethics committee of this medical college.

Inclusion Criteria

Study participants:

Adult patients attending the outpatient department of medicine who were advised thyroid function tests were isolated and only those patients with biochemical evidence of hypothyroidism i.e. low Tri –iodothyronine and Thyroxine levels with increased Thyroid stimulating hormone levels

were enrolled for the study .

Patients in between 20yrs and 60 yrs of age were included.

Both sexes of gender were included.

Thirty numbers of hypothyroid patients with symptoms of peripheral neuropathy were selected for symptomatic group (I) and 30 numbers of hypothyroid patients without any symptoms of peripheral neuropathy were selected for asymptomatic group (II). And they were asked all about the history of hypothyroidism and neurological symptoms. Then clinical examination was done in view of the inclusion and exclusion criteria, such as follows

Symptomatic Group

	Positive Symptoms	**Negative Symptoms**
Sensory	Pain	Numbness
	Tingling	Lack of feeling
Motor	Cramps	Weakness
	Fasciculations	Atrophy (18)

Exclusion Criteria

- Hypothyroid patients with other co morbidity like DM, Alcoholism, HIV, Drug and Toxin induced peripheral neuropathy.
- Age group less than 20years and more than 60 years.
- Post traumatic neuropathy.
- Pregnancy

Consent:

An informed consent was obtained from each participant.

Methods and Data Collection

In this study after getting consents, 60 adult patients attending the outpatient department of this institute who were advised thyroid function tests were isolated and only those patients with biochemical evidence of

hypothyroidism i.e. low Tri –iodothyronine and Thyroxine levels with increased Thyroid stimulating hormone levels were enrolled for the study.

After excluding the patients as per criteria, histories pertaining to principal symptoms of thyroid disease were obtained. Hypothyroid subjects were asked about their neuromuscular symptoms. Relevant clinical examinations were done in all subjects after relevant history taking.

To avoid bias on serum vitamin b12 non vegetarian are selected.

A. After that, all symptomatic and asymptomatic patients for peripheral neuropathy were asked to come on fasting to give blood sample for serum vitamin b12 levels. Quantitative determination of serum vitamin b12 was done on CLIA (enzyme immunoassay) method. The normal range is 250 to 1100 pg/ml.

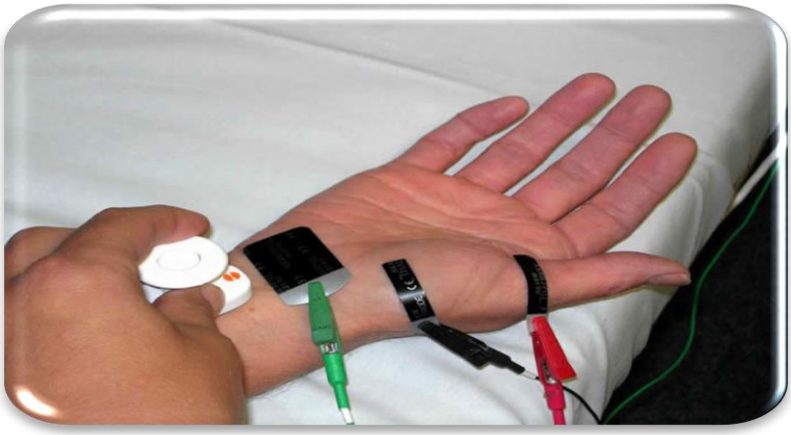
B. Then all symptomatic and asymptomatic patients for peripheral neuropathy were underwent nerve conduction study. The Motor nerves tested were median, ulnar and peroneal. The Sensory nerves studied were median,ulnar and sural.

The parameters studied were distal motor latency, amplitude and conduction velocity for motor nerves. Distal latency, Amplitude, conduction velocity and antidromic study were carried out for sensory nerves. The normal reference values are here:

Nerve	**Conduction velocity (m/s)**	**Latency (s)**	**Amplitude (mv)**
Median Motor	61.5 to 55.0	3.3 to 2.7	17.7 to 11.0
Median sensory	61.0 to 52.6	3.5 to 2.6	15.1 to 7.6
Ulnar Motor	63.7 to 55.5	3.0 to 2.2	7.1 to 4.1
Ulnar Sensory	62.9 to 53.2	3.4 to 2.4	8.2 to 3.6
Peroneal Motor	54.8 to 49.6	4.6 to 3.5	7.2 to 3.0
Sural sensory	61.6 to 53.6	3.5 to 3.0	24.7 to 15.9

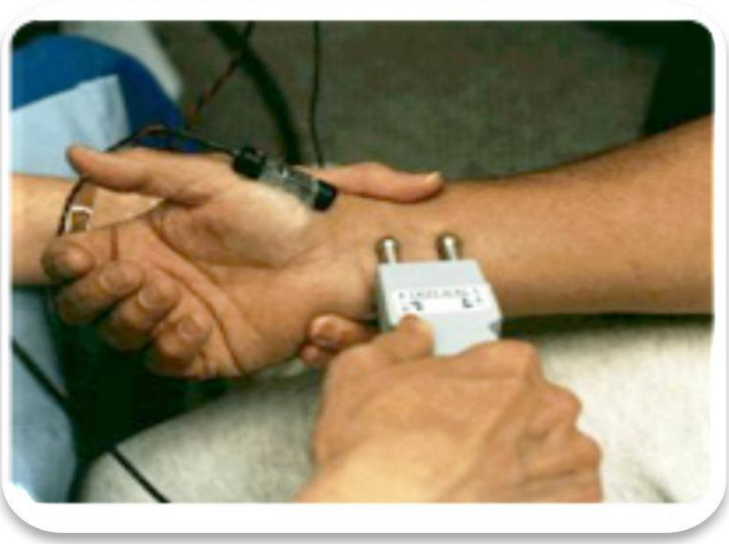
Description of the procedure

- Electrodes
    - Skin will be cleaned
    - Electrodes will be taped to the skin along the nerves that are being studied

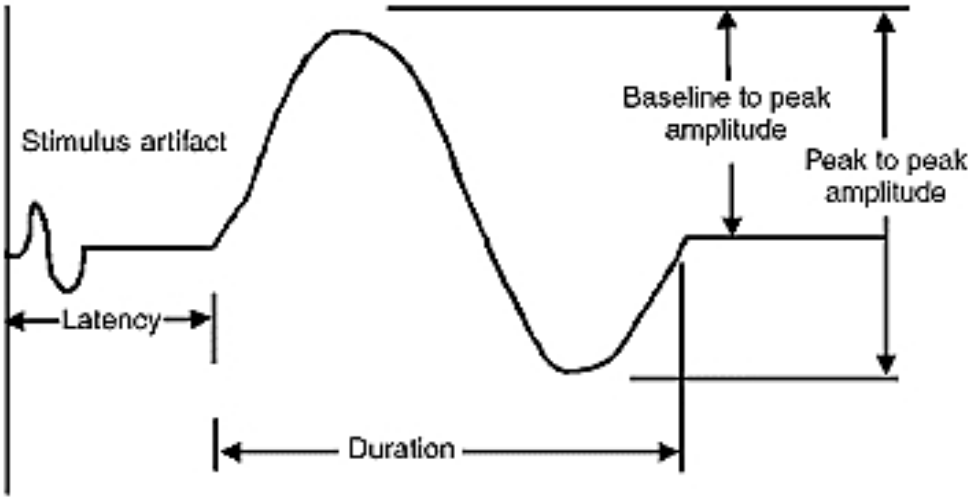


Stimulus

- Small stimulus is applied (electric current) that activate nerves

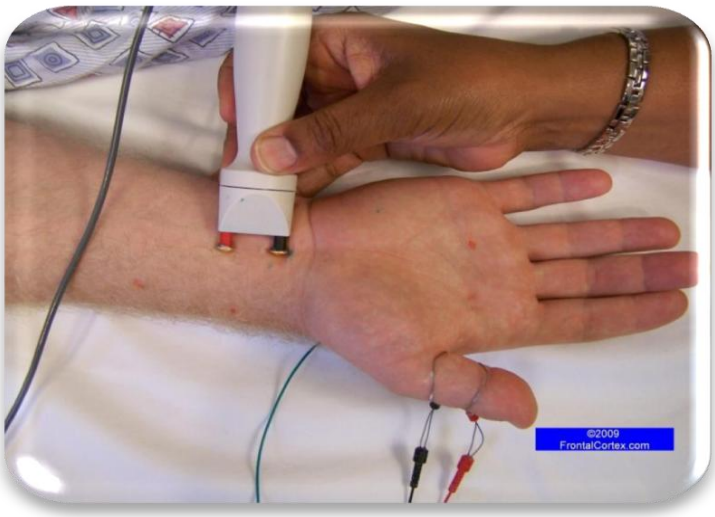


- Current
    - The electrodes will measure the current that travels down the nerve pathway

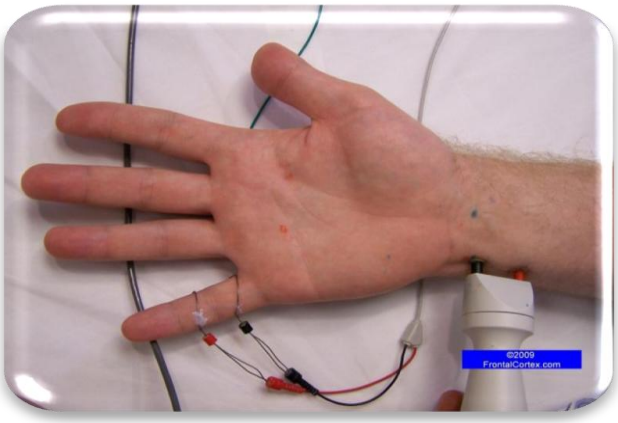


Sensory nerve conduction study

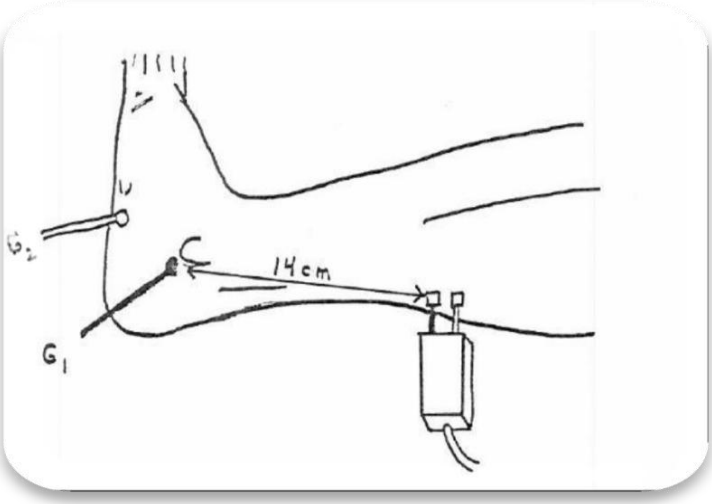
- Median nerves (R & L) at;
    - Index finger humb



- Ulnar nerves (R & L) at;
    - little finger



- Sural nerves (R & L) at;
    - behind the Lateral Malleolus



Statistical Analysis of DATA

The above said all data were collected in excel sheet and a master chart was tabulated .And then analysis was done by using percentages, mean values, standard deviations ,standard error, chi square tests , t tests on SPSS 20 software.

RESULTS AND ANALYSIS

Table 1: Age distribution

AGE	Symptomatic		Asymptomatic		Total	
	n	%	n	%	n	%
20 to 30yrs	3	10.0%	3	10.0%	6	10.0%
31 to 40yrs	19	63.3%	20	66.7%	39	65.0%
41 to 60yrs	8	26.7%	7	23.3%	15	25.0%
Total	**30**	**100%**	**30**	**100%**	**60**	**100%**

Chart 1: Age distribution

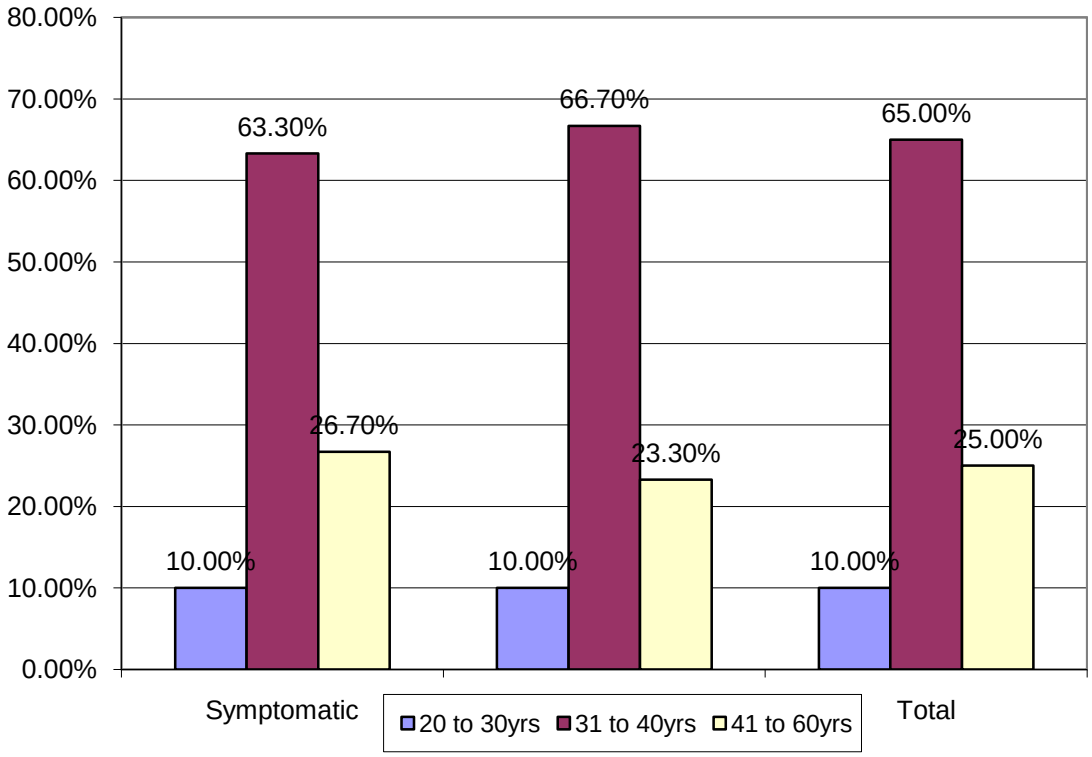


Table 2 : Group distribution of Gender

Sex	Symptomatic		Asymptomatic		Total	
	n	%	n	%	n	%
Male	2	6.7%	2	6.7%	4	6.7%
Female	28	93.3%	28	93.3%	56	93.3%
Total	**30**	**100%**	**30**	**100%**	**60**	**100%**

Chart 2 : Group distribution of Gender

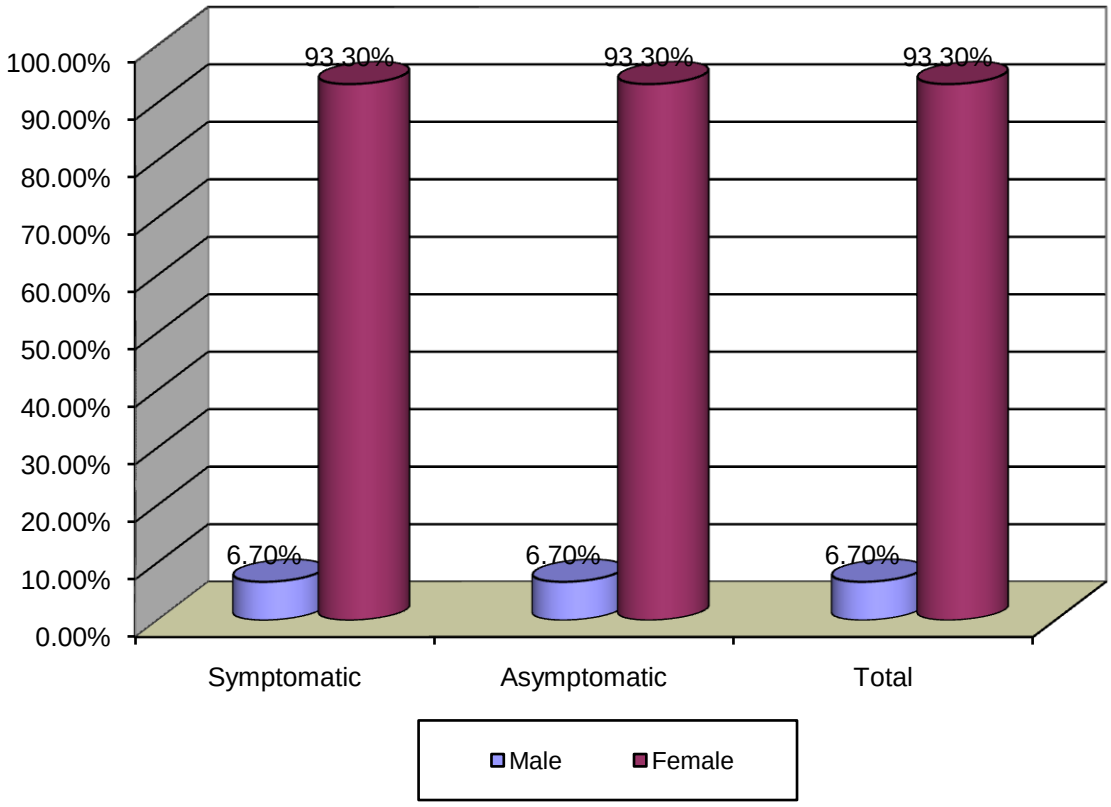


Table 3 : Group distribution of Positive Symptoms

Positive Symptoms	Symptomatic		Asymptomatic		Total		Statistical inference
	n	%	n	%	n	%	
Yes	27	90.0%	0	.0%	27	45.0%	X^2=49.091 Df=1 .000<0.05 Significant
No	3	10.0%	30	100.0%	33	55.0%	
Total	**30**	**100%**	**30**	**100%**	**60**	**100%**	

Chart 3 : Group distribution of Positive Symptoms

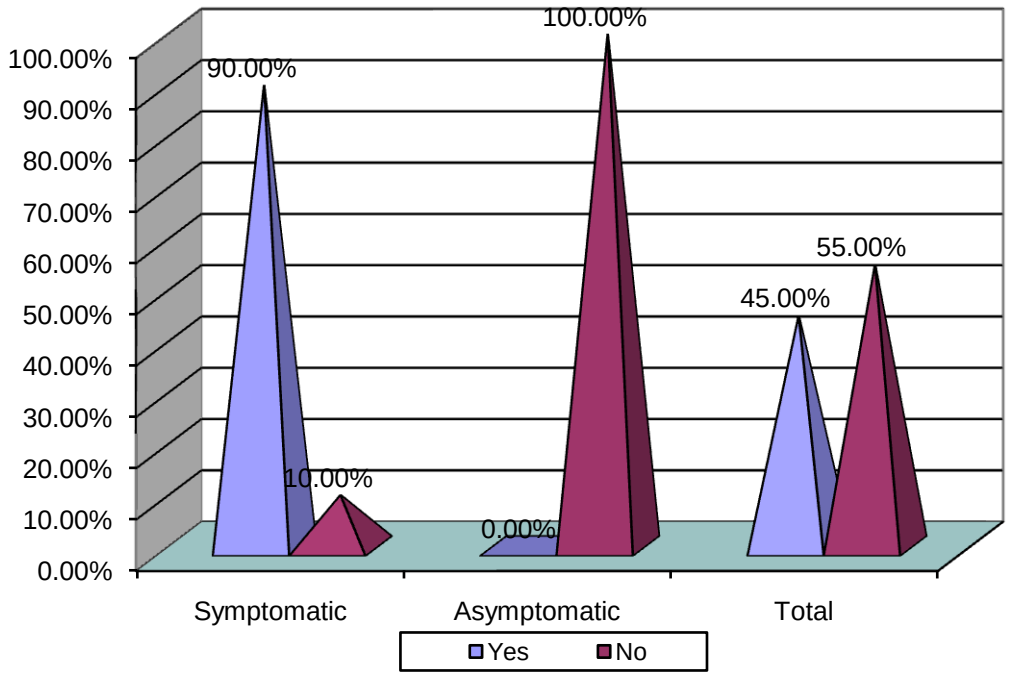


Table 4 : Group distribution of Negative Symptoms

Negative Symptoms	Symptomatic		Asymptomatic		Total		Statistical inference
	n	%	n	%	n	%	
Yes	22	73.3%	0	.0%	22	36.7%	X^2=34.737 Df=1 .000<0.05 Significant
No	8	26.7%	30	100.0%	38	63.3%	
Total	**30**	**100%**	**30**	**100%**	**60**	**100%**	

Chart 4 : Group distribution of Negative Symptoms

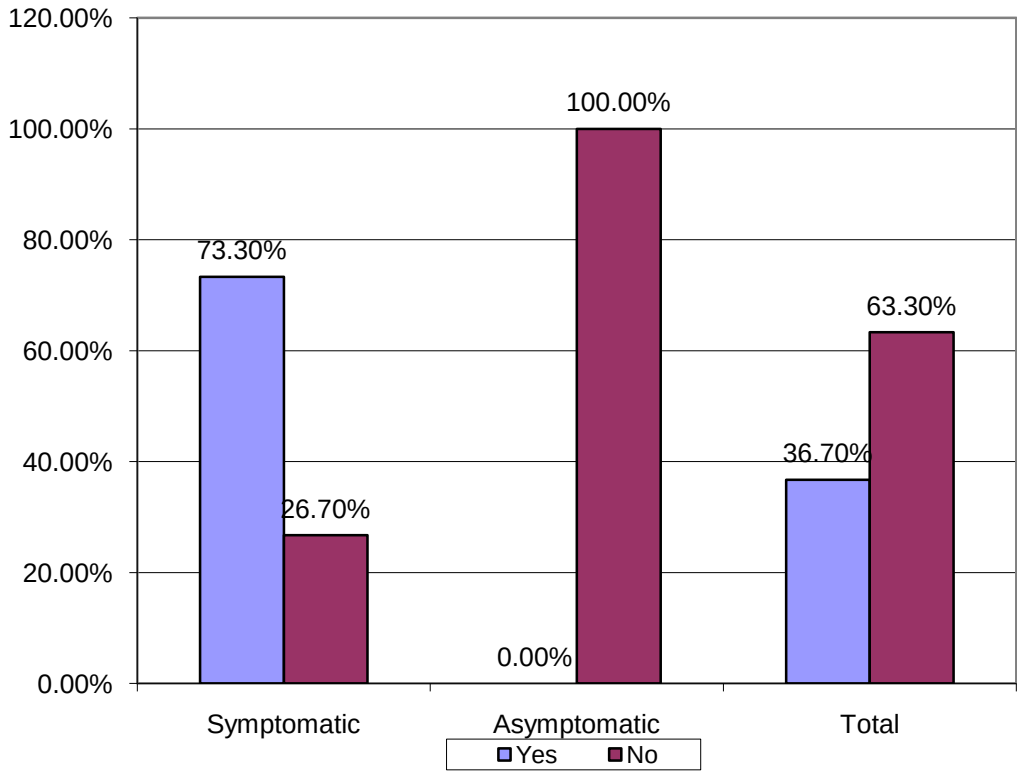
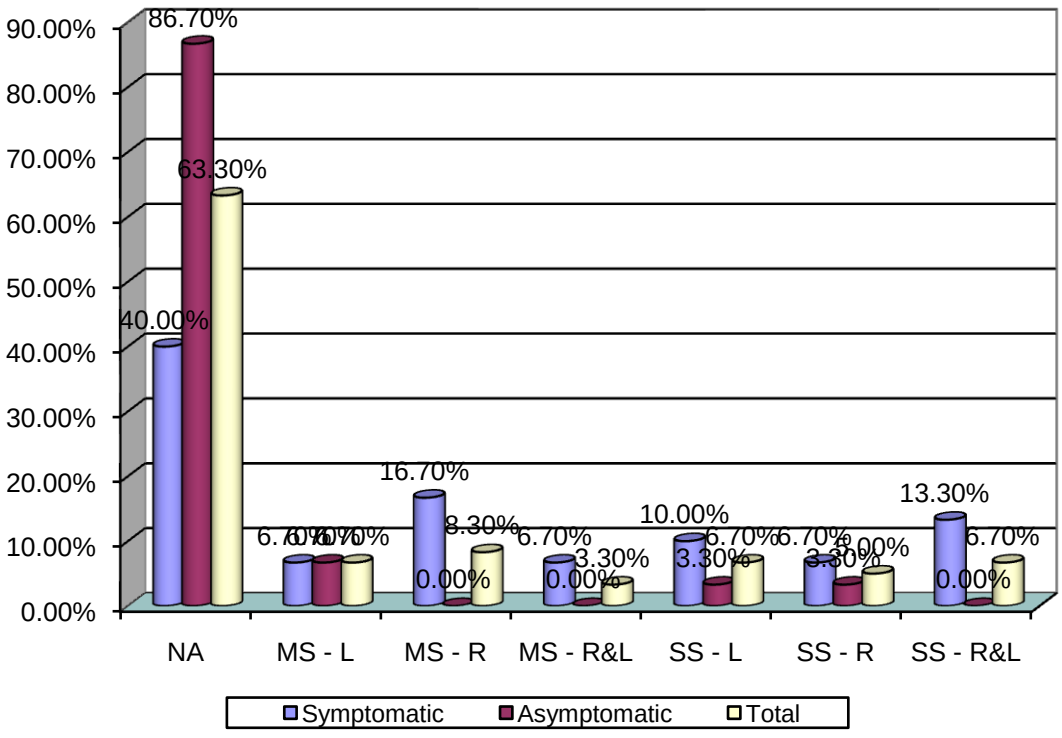


Table 5: NCS Outcome for Nerves

NCS Positivity	Symptomatic		Asymptomatic		Total		Statistical inference
	n	%	n	%	n	%	
NA	12	40.0%	26	86.7%	38	63.3%	X^2=17.491 Df=6 .008<0.05 Significant
MS - L	2	6.7%	2	6.7%	4	6.7%	
MS - R	5	16.7%	0	.0%	5	8.3%	
MS - R&L	2	6.7%	0	.0%	2	3.3%	
SS - L	3	10.0%	1	3.3%	4	6.7%	
SS - R	2	6.7%	1	3.3%	3	5.0%	
SS - R&L	4	13.3%	0	.0%	4	6.7%	
Total	**30**	**100%**	**30**	**100%**	**60**	**100%**	

Chart 5: NCS Outcome for Nerves



MEAN VALUES

	Mean	S.D	Statistical inference
AGE			
Symptomatic (n=30)	37.13	4.384	T=-.030 Df=58 .976>0.05 Not Significant
Asymptomatic (n=30)	37.17	4.211	
DURATION IN MONTHS			
Symptomatic (n=30)	9.27	1.946	T=26.077 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	.00	.000	
SERUM VIT B12 LEVEL pg/ml			
Symptomatic (n=30)	407.10	104.379	T=-4.966 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	580.70	160.517	

Table 5 A: NCS Outcome for Nerves

NERVE CONDUCTION STUDY			
Conduction MM R			
Symptomatic (n=30)	58.1267	1.29533	T=-2.246 Df=58 .029<0.05 Significant
Asymptomatic (n=30)	58.8733	1.27980	
Conduction MM L			
Symptomatic (n=30)	58.0633	1.28506	T=-2.599 Df=58 .012<0.05 Significant
Asymptomatic (n=30)	58.8967	1.19726	
Conduction MS R			
Symptomatic (n=30)	55.7200	3.23423	T=-4.296 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	58.4300	1.21518	
Conduction MS L			
Symptomatic (n=30)	56.0067	2.87941	T=-2.926 Df=58 .005<0.05 Significant
Asymptomatic (n=30)	58.0067	2.39337	
Conduction UM R			
Symptomatic (n=30)	59.3333	2.12170	T=-3.176 Df=58 .002<0.05 Significant
Asymptomatic (n=30)	60.7567	1.23391	
Conduction UM L			
Symptomatic (n=30)	59.5533	1.66562	T=-3.102 Df=58 .003<0.05 Significant
Asymptomatic (n=30)	60.7333	1.25157	

Conduction US R			
Symptomatic (n=30)	58.3000	2.07763	T=-2.645 Df=58 .010<0.05 Significant
Asymptomatic (n=30)	59.7333	2.11975	
Conduction US L			
Symptomatic (n=30)	58.4533	1.79169	T=-1.958 Df=58 .055>0.05 Not Significant
Asymptomatic (n=30)	59.8000	3.31382	
Conduction PM R			
Symptomatic (n=30)	51.9867	1.51742	T=-1.166 Df=58 .248>0.05 Not Significant
Asymptomatic (n=30)	52.3600	.87832	
Conduction PM L			
Symptomatic (n=30)	51.6400	.73607	T=-2.639 Df=58 .011<0.05 Significant
Asymptomatic (n=30)	52.2367	.99567	
Conduction SS R			
Symptomatic (n=30)	55.7133	2.92348	T=-2.664 Df=58 .010<0.05 Significant
Asymptomatic (n=30)	57.3900	1.82669	
Conduction SS L			
Symptomatic (n=30)	55.5700	3.11073	T=-3.153 Df=58 .003<0.05 Significant
Asymptomatic (n=30)	57.6333	1.77964	

Latency MM R			
Symptomatic (n=30)	2.9400	.12205	T=-1.893 Df=58 .063>0.05 Not Significant
Asymptomatic (n=30)	2.9933	.09444	
Latency MM L			
Symptomatic (n=30)	2.9033	.14967	T=-1.322 Df=58 .191>0.05 Not Significant
Asymptomatic (n=30)	2.9500	.12247	
Latency MS R			
Symptomatic (n=30)	3.1100	.51149	T=1.346 Df=58 .184>0.05 Not Significant
Asymptomatic (n=30)	2.9767	.18134	
Latency MS L			
Symptomatic (n=30)	2.9600	.47095	T=-.158 Df=58 .875>0.05 Not Significant
Asymptomatic (n=30)	2.9767	.33185	
Latency UM R			
Symptomatic (n=30)	2.8200	.14716	T=-2.560 Df=58 .013<0.05 Significant
Asymptomatic (n=30)	2.9100	.12415	
Latency UM L			
Symptomatic (n=30)	2.7733	.20500	T=-1.924 Df=58 .059>0.05 Not Significant
Asymptomatic (n=30)	2.8567	.11943	

Latency US R			
Symptomatic (n=30)	2.9267	.15742	T=-1.049 Df=58 .299>0.05 Not Significant
Asymptomatic (n=30)	2.9667	.13730	
Latency US L			
Symptomatic (n=30)	2.9633	.31126	T=-.107 Df=58 .915>0.05 Not Significant
Asymptomatic (n=30)	2.9700	.13933	
Latency PM R			
Symptomatic (n=30)	3.9500	.21294	T=-2.786 Df=58 .007<0.05 Significant
Asymptomatic (n=30)	4.1133	.24031	
Latency PM L			
Symptomatic (n=30)	3.8933	.24059	T=-3.465 Df=58 .001<0.05 Significant
Asymptomatic (n=30)	4.0700	.14179	
Latency SS R			
Symptomatic (n=30)	3.4967	.40214	T=3.141 Df=58 .003<0.05 Significant
Asymptomatic (n=30)	3.2300	.23364	
Latency SS L			
Symptomatic (n=30)	3.4433	.44075	T=2.675 Df=58 .010<0.05 Significant
Asymptomatic (n=30)	3.2067	.20160	

Amplitude MM R			
Symptomatic (n=30)	14.3300	.62981	T=-3.674 Df=58 .001<0.05 Significant
Asymptomatic (n=30)	14.9867	.74959	
Amplitude MM L			
Symptomatic (n=30)	14.3467	.52571	T=-3.442 Df=58 .001<0.05 Significant
Asymptomatic (n=30)	14.9367	.77792	
Amplitude MS R			
Symptomatic (n=30)	10.8500	2.42896	T=-3.966 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	12.8067	1.18407	
Amplitude MS L			
Symptomatic (n=30)	10.9333	2.34158	T=-3.876 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	12.7633	1.09780	
Amplitude UM R			
Symptomatic (n=30)	5.6467	.52702	T=-1.918 Df=58 .060>0.05 Not Significant
Asymptomatic (n=30)	5.9100	.53650	
Amplitude UM L			
Symptomatic (n=30)	5.6033	.56720	T=-.889 Df=58 .378>0.05 Not Significant
Asymptomatic (n=30)	5.7367	.59393	

Amplitude US R			
Symptomatic (n=30)	5.7233	1.12730	T=-1.414 Df=58 .163>0.05 Not Significant
Asymptomatic (n=30)	6.1233	1.06307	
Amplitude US L			
Symptomatic (n=30)	5.8067	1.03622	T=-1.551 Df=58 .126>0.05 Not Significant
Asymptomatic (n=30)	6.2033	.94303	
Amplitude PM R			
Symptomatic (n=30)	4.9467	1.07567	T=-2.421 Df=58 .019<0.05 Significant
Asymptomatic (n=30)	5.5133	.69765	
Amplitude PM L			
Symptomatic (n=30)	5.2367	3.18266	T=-.127 Df=58 .900>0.05 Not Significant
Asymptomatic (n=30)	5.3133	.91415	
Amplitude SS R			
Symptomatic (n=30)	19.5900	1.98448	T=-4.376 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	21.3267	.88743	
Amplitude SS L			
Symptomatic (n=30)	19.4367	1.91698	T=-4.647 Df=58 .000<0.05 Significant
Asymptomatic (n=30)	21.2833	1.03060	

Table 6: NCS Outcome for groups

NCS Positivity	Symptomatic		Asymptomatic		Total		Statistical inference
	n	%	n	%	n	%	
Negative	12	40.0%	26	86.7%	38	63.3%	X^2=14.067 Df=1 .000<0.05 Significant
Positive	18	60.0%	4	13.3%	22	36.7%	
Total	**30**	**100.0%**	**30**	**100.0%**	**60**	**100.0%**	

Chart 6: NCS Outcome for groups

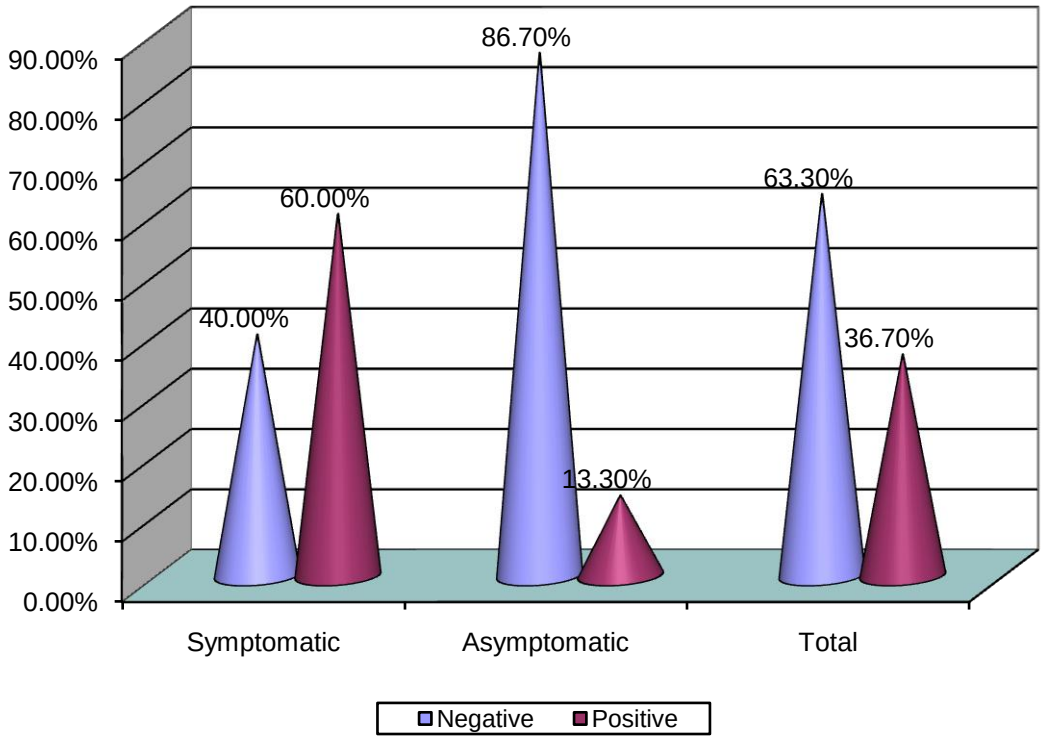


Table 7:Serum vitamin B12 and NCS positivity in Symptomatic (n=30)

SERUM VIT B12 LEVEL pg/ml	Mean	S.D	SS	DF	Ms	Statistical inference
Between Groups			70173.233	6	11695.539	F=1.094 .395>0.05 Not Significant
NA (n=12)	359.33	95.115				
MS – L (n=2)	427.00	9.899				
MS – R (n=5)	389.80	107.272				
MS - R&L (n=2)	477.00	93.338				
SS – L (n=3)	476.00	82.831				
SS – R (n=2)	416.00	199.404				
SS - R&L (n=4)	471.00	112.466				
Within Groups			245783.467	23	10686.238	

T-Test

SERUM VIT B12 LEVEL pg/ml	Mean	S.D	Statistical inference
Negative (n=12)	359.33	95.115	T=-2.174 Df=28 .038<0.05 Significant
Positive (n=18)	438.94	100.238	

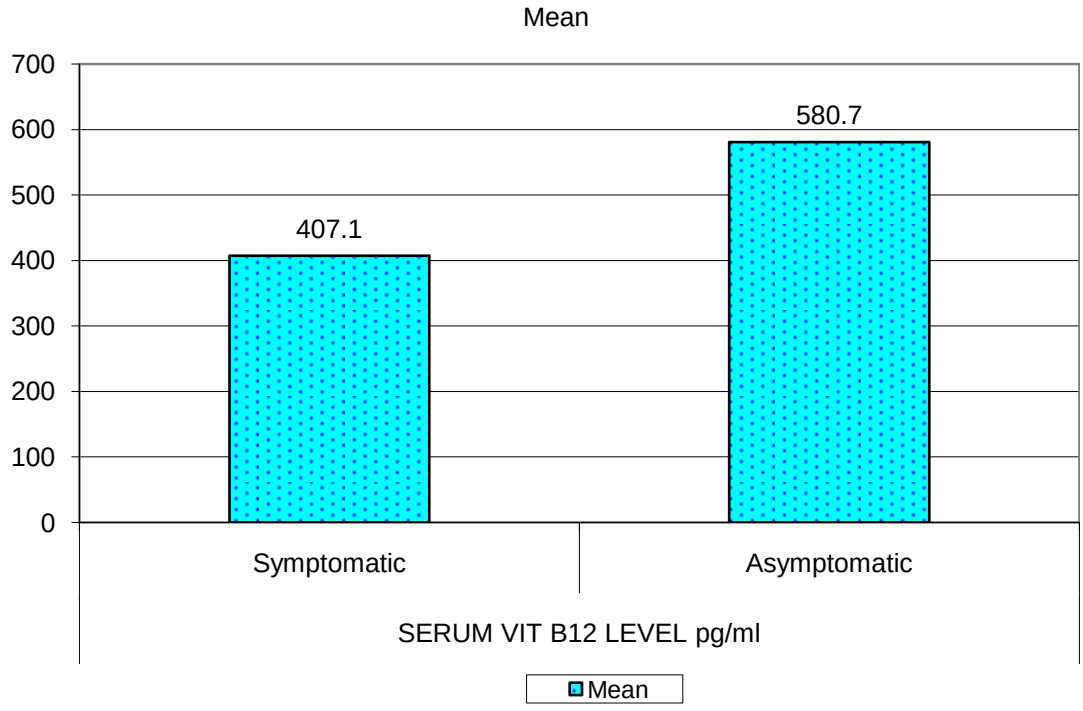
Table 8: Serum vitamin B12 and NCS positivity in Asymptomatic (n=30)

SERUM VIT B12 LEVEL pg/ml	Mean	S.D	SS	DF	Ms	Statistical inference
Between Groups			144662.262	3	48220.754	F=2.081 .127>0.05 Not Significant
NA (n=26)	588.81	151.364				
MS – L (n=2)	709.00	172.534				
SS – L (n=1)	327.00	.000				
SS – R (n=1)	367.00	.000				
Within Groups			602542.038	26	23174.694	

T-Test

SERUM VIT B12 LEVEL pg/ml	Mean	S.D	Statistical inference
Negative (n=26)	588.81	151.364	T=.699 Df=28 .490>0.05 Not Significant
Positive (n=4)	528.00	232.101	

Chart 8: Serum vitamin B12 among groups



DISCUSSION

This study was done to find out the frequency of peripheral neuropathy in hypothyroidism patients who were symptomatic and asymptomatic for the same by doing nerve conduction study. And to find out any correlation between vitamin B12 levels and peripheral neuropathy among them.

A total of 60 hypothyroid patients, as per criteria 30 patients for Group I -Symptomatic and Group II – Asymptomatic for peripheral neuropathy were selected and underwent the investigations. The results were collected and analyzed.

Age distribution:

The study group patients were selected from 20 yrs to 60 years of age. In symptomatic group 10% patients were in 20 to 30years range, 63%patients were in 31 years to 40 years range and 26% patients were in 41 years to 60 years range.

In asymptomatic patients 10% patients were in 20years to 30years age group,66% patients were in 31years to 40years of age group and 23% patients were in 41years to 60years age group. The mean age was almost 37.13 years (SD+/- 4.3) in both groups. Table 1 & Chart1.

Gender distribution:

In both symptomatic and asymptomatic groups 7% patients were males and 93% patients were females. Table 2 & Chart2.

Distribution of patients on the basis of symptoms:

As said earlier, patients were asked about their positive and negative symptoms of motor and sensory perceptions. In our study, almost all patients, told about sensory symptoms, of which 19 patients had both positive and negative symptoms, 8 patients had predominant positive symptoms and 3 patients had predominant negative symptoms. Obviously in asymptomatic group none of them had complaints. Table 3&4.

Nerve conduction study results:

Peripheral nervous system dysfunction is an important outcome of thyroid hormone deficiency. In newly diagnosed cases symptoms and signs of mixed neuropathy may predominate initially. The symptoms of peripheral nerve involvement are a fairly sensitive predictor of polyneuropathy.(3, 19)

In our study among symptomatic group, in total ,60% patients showed decreased conduction velocity and increased latency in median nerve and sural nerve sensory electrophysiology which denotes demyelinating peripheral neuropathy. At the same time about 40%

patients had no abnormal nerve conduction study .And the mean value in months for symptoms was 9.27 months (SD +/-1.9). Table 6.

In asymptomatic patients, in total 13% patients had abnormal sensory neural conductions of median and sural nerves suggestive of demyelinating peripheral neuropathy. Table 5 & 5A, Table 6. Chart 6

This is a good thing for early detection of nerve conduction defects even before patients develop symptoms.

Our observations are coinciding with the early studies done by Dr A.A.Asia et al which said that median and sural nerve demyelinating sensory polyneuropathy are common in hypothyroidism(3, 20). In that study , there was slowing of nerve conduction velocity in 71 % patients characteristically for median and sural sensory nerves. (3) Although motor nerve conduction velocity could be within a normal range sensory nerve action potentials are reduced at an early phase of the disease.(21)

And our study has a similar inference with the study by Dr Sachin pawar by the way early nerve conduction study is very useful to find out peripheral neuropathy in advance.(22)

Neurological dysfunction associated with disorders of thyroid gland could be the result of hormonal imbalance or immune mechanism accompanying thyroid disease(23-25) Metabolic alteration in hypothyroidism affects Schwann cells leading to segmental

demyelination which is reflected as a decrease in conduction velocity.(3, 26) Majority of these cases would have gone unnoticed, had only a clinical examination been done. So that , if we screen all the patients of hypothyroidism with NCS , at an early stage, will be helpful to patients.

Serum vitamin B12 level and positive nerve conduction study:

A study by Jabbar et al said that in hypothyroidism patients vitamin b12 were common to that extent of 40% prevalence.(4). In our study , among symptomatic group who were positive for nerve conduction study were having a mean serum vitaminB12 level of 438.94 pg/ml(SD +/- 100.238) and in asymptomatic group with positive nerve conduction studies were having 528pg/ml(SD+/- 232) which were in normal range of serum vitamin B12.Which reveals that there is no positive correlation in this study population .So that,it may be repeated in a large study group for confirmation.

CONCLUSIONS

- There were high frequencies of peripheral neuropathy in hypothyroidism patients.
- Positive findings in NCS were found in 60% patients of symptomatic group and 13% patients of asymptomatic group.
- Most of the patients suffered by demyelinating sensory neuropathy of median nerve or sural nerve or polyneuropathy.
- There was a positive association of nerve conduction study with symptomatic peripheral neuropathy in hypothyroidism patients.
- There was no correlation found in between serum vitamin b12 level and occurrence of peripheral neuropathy in hypothyroidism patients.
- The nerve conduction study will be very much useful to detect peripheral neuropathy early in asymptomatic hypothyroidism patients also.

LIMITATIONS

- This study was done in a small group of people with hypothyroidism with or without symptoms of peripheral neuropathy.
- There was no follow up study done among both symptomatic and asymptomatic patients.
- Repetition of the electro diagnostic study could have helped in evaluating the course of neuromuscular dysfunction in these patients.

BIBLIOGRAPHY

1. Turker H, Turker C, Cengiz N. Neurological complications of hypothyroidism: INTECH Open Access Publisher; 2012.
2. Velayutham K, Selvan SSA, Unnikrishnan AG. Prevalence of thyroid dysfunction among young females in a South Indian population. Indian Journal of Endocrinology and Metabolism. 2015;19(6):781-4.
3. Asia A, Warkar A. Nerve conduction studies in recently diagnosed untreated hypothyroid patients.
4. Jabbar A, Yawar A, Waseem S, Islam N, Ul Haque N, Zuberi L, et al. Vitamin B12 deficiency common in primary hypothyroidism. Journal of the Pakistan Medical Association. 2008;58(5):258.
5. Raizada NTaN. Disorders of Thyroid Glands. In: MUNJAL YP, editor. api text book of medicine. 2. 10 ed: Jaypee Brothers Medical Publishers; 2015. p. 592 - 605.
6. Strachan MWJ, Newell-Price J. In: FRSE BRWBMF, Professor of Endocrinology, Edinburgh; Uo, Honorary Consultant Physician, Royal Infirmary of Edinburgh U, editors. Davidson's Principles and Practice of Medicine. 22 ed. p. 738-48.

7. J. Larry Jameson SJM, Anthony P. Weetman. Disorders of the Thyroid Gland. HARRISONS P r i n c i p l e s o f I n t e r n a l M e d i c i n e. 19 ed2015. p. 2283 - 304.
8. Kumar V, Abbas AK, Aster JC. Robbins basic pathology: Elsevier Health Sciences; 2012.
9. Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine 19/E (Vol.1 & Vol.2). McGraw-Hill Education; 2015. p. 2290.
10. Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine 19/E (Vol.1 & Vol.2). 2015;2.
11. J. Larry Jameson SJM, Anthony P. Weetman. Disorders of the Thyroid Gland. In: Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine 19/E (Vol1 & Vol2)
12. 19 ed2015. p. 2293.
13. Leach JP, Davenport RJ. Neurological disease. In: Colledge NR, Walker BR, Davidson S, Ralston SH, editors. Davidson's Principles and Practice of Medicine. 22 ed: Churchill Livingstone/Elsevier; 2014. p. 1223.

14. Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine 19/E (Vol.1 & Vol.2). 2015;2:267.
15. Leach JP, Davenport RJ. Neurological disease. In: Colledge NR, Walker BR, Davidson S, Ralston SH, editors. Davidson's Principles and Practice of Medicine. 22 ed: Churchill Livingstone/Elsevier; 2014. p. 1224.
16. Anthony A. Amato RJB. Peripheral Neuropathy. In: Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine 19/E (Vol1 & Vol2). 2. 19 ed2015. p. 2683.
17. Anthony A. Amato RJB. Peripheral Neuropathy. In: Kasper DL, Fauci AS, Hauser S, Longo D, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine 19/E (Vol1 & Vol2). 22 ed2015. p. 289-2690.
18. Mallik A, Weir A. Nerve conduction studies: essentials and pitfalls in practice. Journal of Neurology, Neurosurgery & Psychiatry. 2005;76(suppl 2):ii23-ii31.
19. Jabeen AMaS. Peripheral Neuropathy. In: MUNJAL YP, editor. api text book of medicine. 2. 10 ed: Jaypee Brothers Medical Publishers; 2015.

20. Cruz MW, Tendrich M, Vaisman M, Novis SA. Electroneuromyography and neuromuscular findings in 16 primary hypothyroidism patients. Arquivos de neuro-psiquiatria. 1996;54(1):12-8.
21. 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.
22. Donofrio PD, Albers JW. AAEM minimonograph# 34: polyneuropathy: classification by nerve conduction studies and electromyography. Muscle & nerve. 1990;13(10):889-903.
23. Waghmare S, Pajai S, Chaudhari A, Pawar S, Shende V, Sewagram W. Motor neuropathy in hypothyroidism: A case-control study. Health. 2015;3(3).
24. Duyff RF, Van den Bosch J, Laman DM, van Loon B-JP, Linssen WH. Neuromuscular findings in thyroid dysfunction: a prospective clinical and electrodiagnostic study. Journal of Neurology, Neurosurgery & Psychiatry. 2000;68(6):750-5.
25. Torres C, Moxley R. Hypothyroid neuropathy and myopathy: clinical and electrodiagnostic longitudinal findings. Journal of neurology. 1990;237(4):271-4.

26. Henchey R, Cibula J, Helveston W, Malone J, Gilmore R. Electroencephalographic findings in Hashimoto's encephalopathy. Neurology. 1995;45(5):977-81.

27. Yeasmin S, Begum N, Begum S, Rahman SMH. Sensory neuropathy in hypothyroidism: Electrophysiological and clinical findings. Journal of Bangladesh Society of Physiologist. 2007;2:1-6.

PROFORMA

"A nerve conduction study in Hypothyroid patients with symptomatic Vs asymptomatic peripheral neuropathy in correlation with serum vit B12 level".

1. Name :
2. Age:
3. Sex
4. Occupation:
5. Education :
6. Address:
7. Complaints of pheripheral neuropathy:
8. Symptomatic: Y / N
9. Duration of symptoms:
10. Serum vitamin B12 level:
11. Nerve conduction study:

Nerve	**Conduction velocity (m/s)**	**Latency (s)**	**Amplitude (mv)**
Median Motor			
Median sensory			
Ulnar Motor			
Ulnar Sensory			
Peroneal Motor			
Sural sensory			

PATIENT CONSENT FORM

"A nerve conduction study in Hypothyroid patients with symptomatic vs asymptomatic peripheral neuropathy in correlation with serum vit B12 level"

Patient's name :

Age / Sex :

Occupation :

Education :

Address :

I _____ have been completely explained about the study in the language. I best understand and I am willing to give the all the required information and to undergo all the investigation necessary for the study.

Signature

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு :

கி.ஆ.பெ.விஸ்வநாதம் அரசு மருத்துவக் கல்லூரி மற்றும் மகாத்மாகாந்தி நினைவு அரசு மருத்துவமனை, திருச்சி பொது மருத்துவப் பிரிவில் **தைராய்டு ஹார்மோன் குறைவாக உள்ளவர்களுக்கு ஏற்படும் நரம்பு வியாதியையும், வைட்டமின் B12 அளவையும் ஒப்பு நோக்கும் ஆய்வு**

பெயர் : **தேதி** :

வயது : **இனம்** :

ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாகவும் தெளிவாகவும் எனக்கு விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்து கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் பங்குபெறுகிறேன் மற்றும் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்து கொண்டேன்.

இந்த ஆராய்ச்சியினால் ஏற்படும் நன்மைகள் பற்றிதெளிவாக மருத்துவர் மூலம் தெரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

நாள்:

இடம்:

KEY TO MASTER CHART

NCS	:	NERVE CONDUCTION STUDY
MM R	:	MEDIAN NERVE MOTOR RIGHT
MML	:	MEDIAN NERVE MOTOR LEFT
MSR	:	MEDIAN NERVE SENSORY RIGHT
MSL	:	MEDIAN NERVE SENSORY LEFT
UMR	:	ULNAR NERVE MOTOR RIGHT
UML	:	ULNAR NERVE MOTOR LEFT
USR	:	ULNAR NERVE SENSORY RIGHT
USL	:	ULNAR NERVE SENSORY LEFT
PMR	:	PERONEAL NERVE MOTOR RIGHT
PML	:	PERONEAL NERVE MOTOR LEFT
SSR	:	SURAL NERVE SENSORY RIGHT
SSL	:	SURAL NERVE SENSORY LEFT