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# A Comparative Study of Changes in Nerve Conduction Velocity among Subclinical Hypothyroid Patients and Normal Individuals

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***Abstract**: Sub clinical hypothyroidism (SCH), also called mild hypothyroidism is a term used for a condition in which there are small elevations in Thyroid stimulating hormone (TSH), yet normal circulating levels of thyroid hormones and is essentially a laboratory diagnosis. Effect of SCH on peripheral nerves and muscles has been a matter of debate and conflicting results have been found by different workers. The purpose of this study was to find any abnormality in nerve function that may occur in patients of SCH, by the help of nerve conduction study, which will contribute to early diagnosis and further management. Nerve conduction study of median nerve, sural nerve and tibial nerve was carried on 30 newly diagnosed SCH patients, and 30 age and sex matched healthy control in a time span of one year after taking proper consent from individuals and concerned authority. Statistical analysis of the obtained data showed a positive correlation between TSH and median sensory latency and negative correlation with median sensory amplitude. There is negative correlation between TSH value and sural amplitude and no correlation was found with respect to TSH and motor latency and amplitude.*

***Keywords:** subclinical hypothyroidism (SCH), Nerve conduction velocity (NCV), Thyroid stimulating hormone(TSH)*

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## I. Introduction

Hypothyroidism is a clinical disorder due to the deficiency of thyroid hormone. This hormone is a key regulator of cellular metabolism in our body. In India, about 42 million people suffer from thyroid disorders (1).Thyroid hormone influences the functioning of nearly all organ systems throughout lifetime. Subclinical hypothyroidism (SCH) is defined by the finding of elevated serum TSH concentrations associated with normal free thyroid hormone levels. It affects 3 –8% of the adult population and its prevalence increases after the age of 35years (2). Subclinical hypothyroidism is a state of mild thyroid failure, is asymptomatic and is essentially based on a laboratory diagnosis (3). However the clinical significance of SCH has not been fully characterized.Thyroid hormones exert multiple effects on the neuromuscular system and the brain, with the most important being their role in stimulating the development and differentiation of the neuromuscular system and brain in fetal and neonatal life. Usually hypothyroidism has both central and peripheral involvement. Peripheral polyneuropathy, a progressive nerve disorder, becomes a chronic disability which may be due to defect in axons, nerve cell body or myelin sheath. The metabolic alteration which is caused by hormonal imbalance affects the Schwann cells which induce a segmental demyelization(4). Most of the neuropathy remains latent in the early stage of the disease and it can be investigated using Electroneurogram, which is a noninvasive electrodiagnostic study of nervous system. It assesses the functional integrity of sensorimotor electrical conduction. Effect of subclinical hypothyroidism on the peripheral nervous system has been a matter of debate. There has been evidence suggesting the existence of neuromuscular symptoms and signs in subclinical hypothyroidism, while some studies did not report any peripheral nerve involvement. Motor nerve conduction Study performed by electrical stimulation of a peripheral nerve and recording from a muscle supplied by this nerve is characterized by its Latency, amplitude, and conduction velocity. Latency in milliseconds is the time from the onset of stimulus to the point of take-off from baseline and is an index of speed of impulse travel (5). Amplitude in mV is the size of the response and denotes the density of nerve fibres. Conduction Velocity in meters per second reflects the fastest motor axon. Sensory Nerve conduction is obtained by directly stimulating a sensory nerve and recording directly from it or by its branches. Here too latency, amplitude and conduction velocity are studied (6).The interpretation of Nerve conduction studies is complex. There may be generalized or focal peripheral neuropathy evident from the nerve affected and changes in latencies, amplitude and conduction velocity. Thus we can see that Hypothyroidism is a common endocrinal disorder and overt hypothyroidism is

associated with peripheral neuropathy. But conflicting results regarding the peripheral neuropathy in subclinical hypothyroidism exists. This study proposes to identify the neurological deficit in peripheral nerves in subclinical hypothyroidism, if any, with the help of nerve conduction study.

## II. Materials And Methods:

This cross-sectional study was carried in Medical College, Kolkata on 30 newly diagnosed subclinical hypothyroid patients, selected as study group and 30 healthy subjects as control. The study was conducted in a time span of 1 year after taking institutional ethical clearance and informed consent from subjects.

**Inclusion criteria**: Subclinical hypothyroid(TSH $\geq$ 6 & normal $FT_4$, $FT_3$) patients, aged between 20 years and 60 years attending general OPD, Medicine OPD & Endocrine OPD.

**Exclusion criteria**: Cases with h/o CVA, CAD and Neuropathy, Hypertensives, Diabetics, patients with chronic renal disease and patients with history of hepatic disease.

Blood samples were sent for estimation of TSH, $FT_4$ & $FT_3$ from the NABL accredited Biochemistry laboratory of Medical college, Kolkata by fully automated immunoassay analyzer

Using commercial kit ERBA. Nerve conduction study was done in the department of Physiology & department of Neuromedicine, for estimation of Latency, Amplitude and Conduction velocity of motor nerve(Median nerve and Tibial nerve) and only latency and amplitude of sensory nerve(median and Sural nerve)by"RMSALLERON201-2CH EMG, NCV-ET SYSTEM" of same institution.

Patients were were asked to report to the Biochemistry Department, the next day on empty stomach.10 ml of blood was withdrawn from patients of subclinical hypothyroidism and normal healthy subjects after overnight fasting with dry disposable syringe and needle, under all aseptic conditions by venipuncture in the antecubital vein in sterile and dry vial. The blood samples were incubated at $37^0$ C temperature for 25-30 minutes for proper clot formation and these blood samples then centrifuged at 3000rpm for 10 minutes for serum preparation. This serum samples were used for biochemical assays.

**Procedure:** After all of the electrodes were in place, the instrument was set to deliver repetitive stimuli, usually at 1 Hz. The stimulus voltage was initially set to zero, then gradually increased with successive stimuli. A compound muscle action potential (CMAP) appeared, that grew larger with the increasing stimulus voltage. Eventually, further increases in voltage did not cause any change in CMAP amplitude. A stable response was assured if the voltage is 25% greater than the voltage needed to produce the highest amplitude CMAP. Once a good recording was made, the trace was stored for later analysis and the stimulating electrode moved proximally to a second stimulus site. Most nerves were stimulated in two sites for motor nerve conductions, but some were stimulated in at least three locations along the course of the nerve .

**Interpretation**: The following measurements were made from the CMAP produced by stimulation at each site: Latency from stimulation to onset of the CMAP, Latency from stimulation to peak of the CMAP, CMAP amplitude. The distance between stimulus sites was measured, and the NCV calculated according to the following simple formula: NCV = Dist/(PL−DL).Where Dist = distance, PL = proximal latency, and DL = distal latency. The final results were expressed as meters per second or m/s.

**Statistical analysis:** After collection, data were tabulated in Microsoft Office Excell 2010 and analysis was performed by using IBM SPSS Statistics (Version21). The baseline data were analyzed by descriptive statistics and then thyroid profile, and NCS parameters were analyzed by independent T test. Data were presented as mean ±SD. Pearson's correlation analysis (including coefficient r and two-tailed P value ) was performed to assess the relationship

between TSH and NCS parameters,. P value less than 0.05 considered statistically significant, r value ranges from -1 to +1.

## III. Results And Analysis:

**Table1:** Thyroid Profile Test

| | Case(N=30) | | Control(N=30) | | |
|---|---|---|---|---|---|
| Variable | Mean | Std. dev. | Mean | Std.dev. | P value |
| TSH | 9.72 | 2.19 | 2.45 | 0.93 | 0.000 |
| T3 | 2.64 | 0.77 | 2.53 | 0.44 | 0.52 |
| T4 | 1.29 | 0.25 | 1.30 | 0.27 | .842 |

Table 1 shows TSH is higher in Case, and there is no significant difference in $T_3$& T4 values of cases and

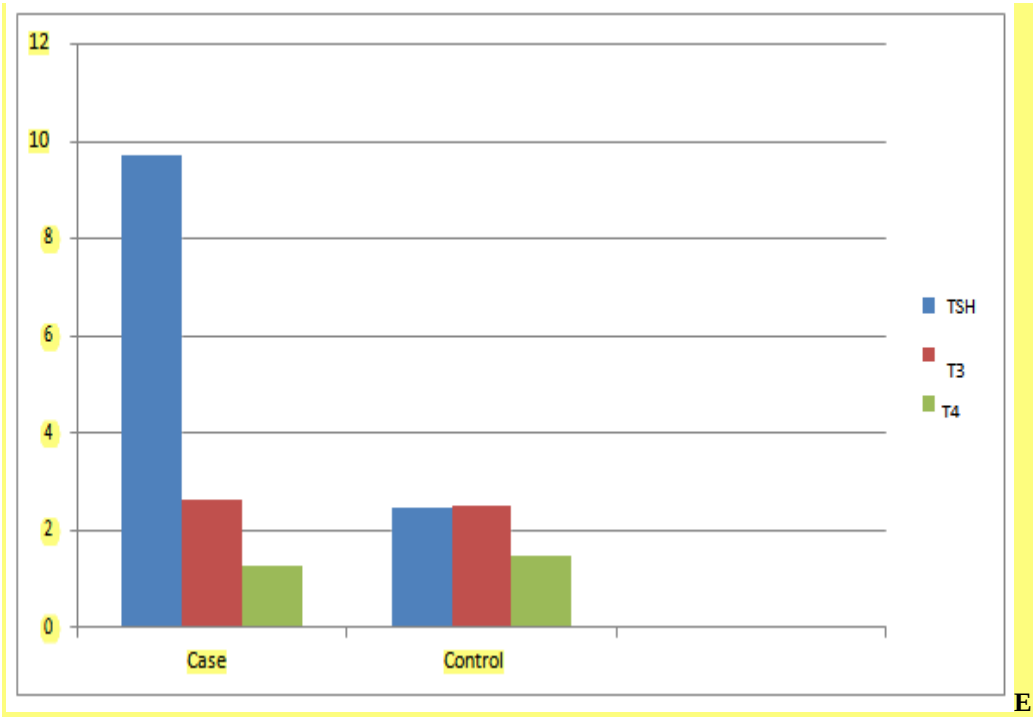


**FIGURE 1.** Shows a significant rise of TSH in cases compared to control while there is no difference in $T_3$ and $T_4$

**Table 2:** Gender distribution

| Age | Case | Control |
|---|---|---|
| male | 30% | 66.66% |
| female | 70% | 33.33% |

Table 2 shows incidence of SCH in females is higher

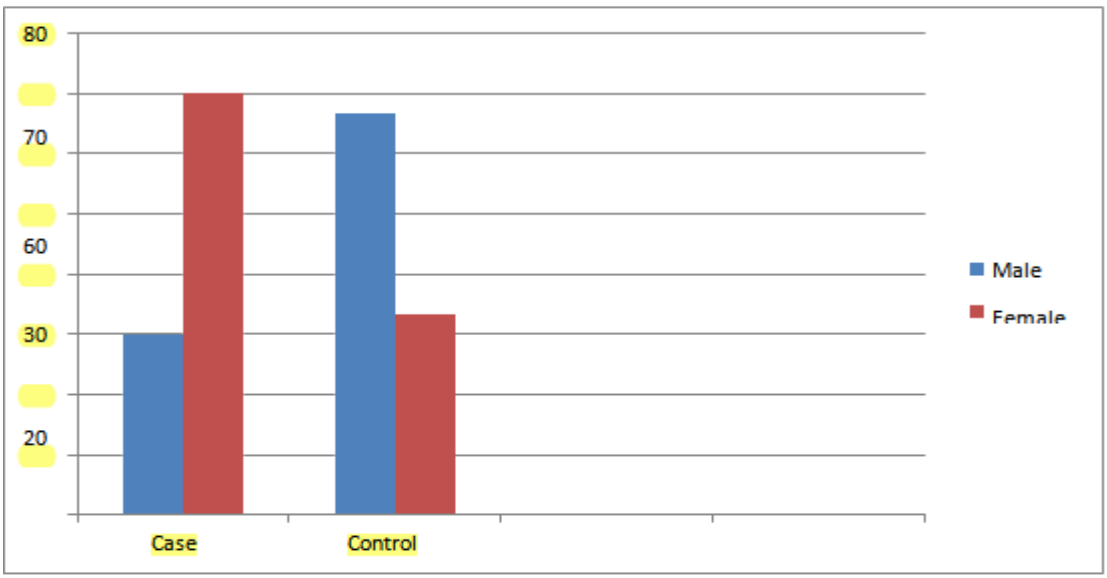


**Figure: 2** shows incidence of SCH is more in females

**Table 3:** Age Distribution (in years)

| | Case | | Control | | |
|---|---|---|---|---|---|
| Variable | mean | Std. dev. | Mean | Std. dev. | P value |
| Age | 36.733 | 10.91 | 37.333 | 9.20 | 0.819 |

Table 3 shows that the age distribution is similar in both the groups

**Table 4**: Motor Parameters of Median Nerve In Case And Control

| | Case | | Control | | |
|---|---|---|---|---|---|
| Variable | mean | Std.dev. | mean | Std.dev. | P value |
| Rt med lat | 5.12 | 0.51 | 5.02 | 0.35 | 0.373 |
| Lt med lat | 5.14 | 0.50 | 5.03 | 0.28 | 0.332 |
| Rt med amp | 9.66 | 2.94 | 10.44 | 1.69 | 0.215 |
| Lt med amp | 9.94 | 3.12 | 10.10 | 1.97 | 0.817 |
| Rt med NCV | 56.25 | 4.66 | 59.61 | 2.88 | 0.001 |
| Lt med NCV | 57.48 | 5.52 | 58.36 | 3.83 | 0.475 |

Table 4 shows a significant decrease in Conduction Velocity of Right Median Nerve in Cases while there is no significant change in the Latency and Amplitude

**Table 5**: Motor Parameters of Tibial Nerve In Case And Control

| | Case | | Control | | |
|---|---|---|---|---|---|
| Variable | mean | Std.dev. | mean | Std.dev | P value |
| Rt tibial lat | 7.57 | 0.93 | 7.34 | 0.61 | 0.26 |
| Rt tibial amp | 10.81 | 4.00 | 11.43 | 2.77 | 0.48 |
| Rt tibial NCV | 50.67 | 5.58 | 54.18 | 5.75 | 0.02 |
| Lt tibial lat | 7.32 | 0.90 | 7.12 | 0.63 | 0.303 |
| Lt tibial amp | 11.31 | 3.67 | 11.09 | 1.67 | 0.761 |
| Lt tibial NCV | 49.55 | 5.59 | 52.42 | 5.67 | 0.05 |

Table 5 shows a significant decrease in the Right Tibial Nerve Conduction

**Table 6:** Sensory Parameters of Median Nerve in Case And Control

| | Case | | Control | | |
|---|---|---|---|---|---|
| Variable | Mean | Std.dev. | Mean | Std.dev. | P value |
| Rt med SLAT | 3.14 | 0.50 | 2.69 | 0.37 | 0.000 |
| Lt med SLAT | 3.32 | 0.61 | 2.64 | 0.43 | 0.000 |
| Rt med SNAP | 60.94 | 24.28 | 82.05 | 7.73 | 0.000 |
| Lt med SNAP | 72.98 | 28.29 | 81.72 | 13.14 | 0.131 |

Table 6 shows a highly significant increase in latency of both Right and Left median nerves and a highly significant decrease in amplitude of Right median nerve.

**Table 7:** Parameters of Sural Nerve In Case and Control

| | Case | | Control | | P value |
|---|---|---|---|---|---|
| Variable | Mean | StD.DEV. | Mean | Std.dev. | |
| Rt sural lat | 2.81 | 0.48 | 2.57 | 0.52 | 0.082 |
| Lt sural lat | 2.92 | 0.50 | 2.55 | 0.51 | 0.007 |
| Rt sural amp | 34.15 | 15.1 | 64.50 | 18.03 | 0.000 |
| Lt sural amp | 30.17 | 16.24 | 70.65 | 30.63 | 0.000 |

Table 7 shows a highly significant decrease in Amplitude in both the Sural nerves in the Cases and a highly significant increase in Latency in Left Sural Nerve

**Table 8:** Correlation of TSH and Motor Parameters of Median Nerve

| Variable | r value | P value | Significance |
|---|---|---|---|
| Rt med lat | 0.023 | 0.864 | NS |
| Lt med lat | 0.140 | 0.287 | NS |
| Rt med amp | -0.099 | 0.452 | NS |
| Lt med amp | 0.019 | 0.886 | NS |
| Rt med NCV | -0.348 | 0.006 | S |
| Lt med NCV | -0.078 | 0.553 | NS |

(NS- nnnnot significant , S-significant)

**Table 9:** Correlation between TSH and Motor Parameters of Tibial Nerve

| Variable | r value | P value | significance |
|---|---|---|---|
| Rt tibial lat | 0.121 | 0.358 | NS |
| Rt tibial amp | -0.144 | 0.273 | NS |
| Rt tibial NCV | -0.273 | 0.035 | S |
| Lt tibial lat | 0.022 | 0.865 | NS |
| Lt tibial amp | 0.002 | 0.986 | NS |
| Lt tibial NCV | -0.156 | 0.235 | NS |

**Table 10 :** Correlation between TSH and Parameters of Median Nerve

| Variable | r value | P value | Significance |
|---|---|---|---|
| Rt med SLAT | 0.405 | 0.001 | S |
| Lt med SLAT | 0.508 | 0.000 | S |
| Rt med SNAP | -0.427 | 0.001 | S |
| Lt med SNAP | -0.143 | 0.277 | NS |

**Table 11** : Correlation between TSH and Parameters of Sural Nerve

| Variable | r value | P value | Significance |
|---|---|---|---|
| Lt Sural LAT | 0.241 | 0.063 | NS |
| Lt Sural AMP | -0.590 | 0.000 | S |
| Rt Sural LAT | 0.221 | 0.089 | NS |
| Rt Sural AMP | -0.662 | 0.000 | S |

## IV. Discussion:

SCH is defined as a high serum TSH concentration with normal serum free Thyroxine and free Triiodothyronine concentrations associated with few or no signs and symptoms of hypothyroidism. It's incidence increases with age, female gender and greater dietary iodine uptake.

Various studies have shown that SCH is associated with neuromuscular symptoms and decrease in quality of life with progression to overt hypothyroidism (7). Due to apparently asymptomatic nature of the illness, the "American Thyroid Association" (ATA) has recommended routine population screening of both sexes at age of 35 years and then every 5 years thereafter for early detection and treatment of SCH(8). In the literature, two types of abnormality of the PNS in hypothyroidism have been described. The first is a mononeuropathy, due to mucinous deposits which cause nerve damage through a compression mechanism(9), second is a sensorimotor polyneuropathy. Morphologically some studies have shown a primary involvement of myelin (10) while more recent studies have shown primary axonal damage (11).The axonal loss or demyelination of nerves which results in peripheral neuropathy can be effectively revealed by NCV studies in patients of hypothyroidism. As most of the neuropathy remain latent in SCH, we undertook Nerve Conduction Studies to find out if any involvement of the peripheral nerves had taken place or not.

Table 4 & 5 show a significant decrease in conduction velocity of motor median and tibial nerves. A significant increase in latency was found in sensory median nerve and sural nerve. A significant decrease in amplitude in sural nerve which is a purely sensory nerve was also recorded. Table 8, 9, 10,11 show the correlation between TSH and the different NCV parameters. Table 8 & 9 show a negative correlation between TSH and motor median and tibial nerve conduction velocity which means, as the level of TSH increases, the conduction velocity decreases.There is positive correlation between TSH and median sensory latency and negative correlation with median sensory amplitude ( table 10).There is also negative correlation between TSH and sural amplitude (table 11).No correlation was found with respect to TSH and motor latency and amplitude.Contrary to our findings, Ozata M et al in 1995 (12) found that subclinical hypothyroidism of short duration does not lead to abnormalities of peripheral nerves.Waghmare et al (2015)(13) observed significant prolonged latencies and reduced amplitude and conduction velocity in motor nerves and we also observed a decrease in conduction velocity in motor nerves. Similar findings were found by Rao et al (1980)(14) and they also reported increased latency in sensory nerve. Adikesevan Balaraman et al in 2013 (15) found significant decrease in sensory nerve area but non- significant decrease in conduction velocity in median nerve in subclinical hypothyroid patients. He also found decrease in area & conduction velocity in sural nerve.

The present study shows that there is a sensorimotor poly neuropathy in SCH. A decrease in conduction velocity of motor nerves was observed and it is a well-known fact that conduction velocity is determined by myelination, diameter and length of the axon (16). Thyroid hormones also have profound effects on mitochondrial oxidative activity is a well established fact(17) and so demyelination due to oxidative damage to myelin membrane or oligodendroglial cells may result in decrease in nerve conduction velocity. A prolonged latency and decreased amplitude were observed in the sensory nerves in a previous study by Misiunas et al in 1991(18).Similar alterations in the amplitude and latencies occurred in the longer nerves like sural. The subclinical neuropathies of hypothyroid subjects are characterized by prolonged distal latencies, which is consistent with our study.

Amplitude represents the number of activated axons and they are one of the earliest parameters affected in axonal neuropathies. Involvement of sensory nerve may be due to axonal degeneration of sensory nerve. Thus it can be said that the presence of electrophysiologic abnormality in SCH suggests that NCV study is of value for the evaluation and early diagnosis of peripheral neuropathy in this condition.

## V. Conclusion

Motor Nerve conduction velocity was decreased in SCH and a negative correlation was found between it and TSH. In the sensory component, there was an increased latency along with a positive correlation between it and TSH in SCH. Amplitude was found to be decreased and a negative correlation was obtained between it and TSH. Thus it can be said that subclinical sensorimotor polyneuropathy develops early in SCH, which can be diagnosed by electroneurological tests. Hence, screening tests need to be implemented in Indian population for

early detection of thyroid disorders and electrophysiological studies are to be conducted in subclinical hypothyroid subjects to detect peripheral neuropathy because early detection may reverse the condition by treatment.

**Limitations**

Studies for SCH should ideally be performed in community population but due to lack of feasibility, we have taken a small sample size.

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