# Nerve Conduction and Heart Rate variability in Patients with Hypothyroidism at a Tertiary Care Centre in Eastern Nepal

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## ABSTRACT

**Introduction:** Thyroid hormone effects on many organs including central and peripheral nervous systems. However, these hormones do not affect all systems/organs to a similar extent. Thus, we conducted this study to explore the effect of thyroid hormones on somatic nervous system assessed by Nerve conduction study and cardiac autonomic activity assessed by heart rate variability.

**Methods:** The study included newly diagnosed hypothyroid patients and healthy controls. In all subjects NCS were performed in median, ulnar, tibial and sural nerves using Nihonkohden machine Cardiac autonomic control was assessed using Short-term Heart Rate Variability and parameters were analyzed by Time Domain and Frequency Domain methods.

**Results:** Both the groups were comparable in term of age, Body Mass Index, Pulse Rate, Systolic Blood Pressure and Diastolic Blood Pressure. Sensory parameters of NCS showed significant decrease in left median nerve SNAP amplitude (38.24±10.23 Vs 31.59±14.06, P=0.048) and nerve conduction velocity of bilateral median nerve in hypothyroid patients. In motor parameters of NCS, onset latencies of bilateral median nerves and right ulnar nerve were significantly increased in hypothyroid patients. All Time Domain measures of HRV and Frequency Domain measures; LF Power, HF Power and Total Power were significantly decreased (P<0.05) in hypothyroid patients. These HRV parameters are indicators of parasympathetic activity.

**Conclusions:** In newly diagnosed hypothyroid patients, especially median nerve functions (both sensory and motor) and parasympathetic activity were decreased. It reflects that in hypothyroidism both autonomic nervous system and other somatic nerves are not affected in a similar extent.

**Keywords:** *hypothyroidism; heart rate variability; nerve conduction study.*

## INTRODUCTION

Thyroxine (T4) and Triiodothyronine (T3) are the two major hormones which are secreted from thyroid gland. Thyroid hormones acts on many organs, including central and peripheral nervous system for maintaining the metabolic homeostasis. Thyroid hormone plays important role in development of central nervous system and in myelination of neurons.

The thyroid hormone also influences the autonomic nervous system. Previous studies have shown sympathovagal imbalance with sympathetic withdrawal and decreased vagal modulation in hypothyroid patients.[1,2] In contrast, other studies have shown that thyroid hormone deficiency is associated with increased sympathetic influence on the cardiovascular autonomic system.[2,3] The literature shows that thyroid hormones are essential for proper health of all the tissue cells.

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It acts differently on different tissue of the body.[4] Therefore we wanted to study its effect on somatic nervous system assessed by Nerve conduction study (NCS) and autonomic nervous system assessed by heart rate variability (HRV) in newly diagnosed hypothyroid patients and healthy control.

## METHODS

This was a descriptive cross sectional study conducted in Department of Basic and Clinical Physiology at B.P.Koirala Institute of Health Sciences from July 2014 to June 2015. The Ethical approval was taken by the Institutional Review Committee and the procedure was explained to the patients recruited for the study and written informed consent was obtained from all the subjects.

The study was conducted in 30 newly diagnosed hypothyroid patients (10 male and 20 female patients) of age ranging between 18-45 years who attended OPD at BPKIHS and 30 healthy subjects for control group which comprises both male and female of similar number and similar age group. Subjects with history of cardiac, renal, hepatic, and mental illness, any acute or chronic illness, diabetes mellitus, alcohol addiction, leprosy, neuromuscular disorders, drug-induced neuropathy, myopathy and those under treatment for hypothyroidism, were excluded. Subjects were advised to come with adequate night sleep.

A detailed history taking and clinical examination were performed using standard proforma. Anthropometric variables, cardiorespiratory variables, HRV and NCS were studied. All the tests were performed between 8-11 am and room temperature of the laboratory was maintained at 26 ± 2 degree Celsius during recording. Blood sample was taken; centrifuged and thyroid function test was done by ELISA. All data were analysed statistically for comparison between the groups.

Recording of HRV: HRV was recorded using Polar S810i heart rate monitor following its standard procedure. The resting cardiac cycle (R-R intervals) signal at spontaneous respiration was recorded for 5 min in supine position after 15 min of supine rest for HRV analysis. The HRV recording was analysed using HRV software (Kubios HRV version 2.1, Kuopio FINLAND).[5]

Recording of Motor NCS: NCS of median, ulnar and tibial nerves of bilateral limb were recorded using Digital Nihon Kohden (NM_420S, H636, Japan) by belly tendon montage. For each site of stimulation, latency and amplitude of CMAP were recorded. Mean latencies of F waves were also recorded.

Recording of Sensory NCS: Antidromic method of stimulation was employed for testing sural nerve and Orthodromic method of stimulation was employed for testing median and ulnar sensory nerves using ring electrodes. Onset latency, SNAP (sensory nerve action potential) amplitude and NCV were recorded.

The statistical analysis was done using SPSS version 11.5. Data of anthropometric variables and NCS variables were normally distributed. Thus, these data were compared between the groups using unpaired t test. The HRV parameters were non-normally distributed. Thus, Mann Whitney U test was used to compare the HRV data between the groups. The P value of $<0.05$ was considered statistically significant with 95% of confidence interval.

## RESULTS

Both the groups were compared in terms of their general characteristics i.e. age, height, weight, body mass index(BMI), upper limb length, lower limb length, systolic blood pressure(SBP), diastolic blood pressure(DBP), respiratory rate and pulse rate (Table 1).

**Table 1. Comparison of general characteristics between hypothyroid patients and healthy controls.**

| General characteristics | Hypothyroid patients n = 30; (Mean ± SD) | Healthy Controls n = 30; (Mean ± SD) |
|---|---|---|
| Age (years) | 31.96 ± 9.12 | 29.27 ± 6.21 |
| Weight (kg) | 62.7 ± 15.93 | 60.10 ± 10.73 |
| Height (cm) | 157.5 ± 5.53 | 159.07 ± 7.060 |
| Body mass index (kg/m$^2$) | 25.14 ± 5.60 | 23.85 ± 4.62 |
| Upper Limb Length (cm) | 68.96 ± 3.34 | 69.07 ± 3.05 |
| Lower Limb Length (cm) | 93.36 ± 4.87 | 93.30 ± 3.75 |
| SBP (mmHg) | 111.2 ± 7.45 | 110 ± 8.3 |
| DBP (mmHg) | 76.66 ± 4.79 | 74.60 ± 5.66 |
| RR (breaths/min) | 18.26 ± 2.54 | 17.40 ± 2.14 |
| PR (beats/min) | 77 ± 7.72 | 74.77 ± 5.53 |

*SBP: Systolic blood pressure, DBP: Diastolic blood pressure, RR=respiratory rate, PR: pulse rate*

On comparison of sensory nerve conduction variables between healthy controls and hypothyroid patients, we found prolonged onset latency in bilateral median nerve, decrease in SNAP amplitude of left median nerve and decrease in conduction velocity of bilateral median

nerve in hypothyroid patients (Table 2.) whereas onset latency, SNAP amplitude and conduction velocity of bilateral ulnar and sural nerves were comparable within the group.

**Table 2. Comparison of sensory parameters of nerve conduction study (NCS) between hypothyroid patients and healthy controls.**

| Sensory parameters of NCS | Hypothyroid patients n = 30; (Mean ± SD) | Healthy controls n = 30; (Mean ± SD) | P value |
|---|---|---|---|
| LMONLAT (ms) | 2.12 ± 0.39 | 1.86 ± 0.238 | 0.003 |
| LMNAMP (mv) | 31.595 ± 14.067 | 38.24 ± 10.23 | 0.048 |
| LMNCV (m/s) | 53.54 ± 8.871 | 60.40 ± 6.57 | 0.001 |
| RMONLAT (ms) | 2.028 ± 0.326 | 1.76 ± 0.202 | 0.001 |
| RMNCV (m/s) | 55.88 ± 8.206 | 62.75 ± 6.069 | 0.001 |

*LMNONLAT: Left median nerve onset latency, LMNAMP: Left median nerve amplitude, LMNCV: Left median nerve conduction velocity, RMNONLAT: Right median nerve onset latency, RMNCV: Right median nerve conduction velocity.*

**Table 3. Comparison of motor parameters of nerve conduction study (NCS) between hypothyroid patients and healthy controls.**

| Motor parameters of NCS | Hypothyroid patients n = 30; (Mean ± SD) | Healthy controls n = 30; (Mean ± SD) | P value |
|---|---|---|---|
| LMNPRONLAT (ms) | 7.093 ± 0.730 | 6.64 ± 0.656 | 0.015 |
| LMNDSONLAT (ms) | 3.163 ± 0.578 | 2.79 ± 0.548 | 0.008 |
| RMNDSONLAT (ms) | 3.05 ± 0.5488 | 2.75 ± 0.532 | 0.024 |
| RUNDSONLAT (ms) | 2.19 ± 0.471 | 2.0 ± 0.301 | 0.043 |
| LTNPRONLAT (ms) | 12.14 ± 1.1.473 | 11.21 ± 1.306 | 0.018 |

*LMNPRONLAT: Left median nerve proximal onset Latency, LMNDSONLAT: Left median nerve distal onset latency, RMNDSONLAT: Right median nerve distal onset latency, RUNDSONLAT: Right ulnar nerve distal onset latency, LTNPRONLAT: Left tibial nerve proximal onset latency.*

On comparison of motor nerve conduction variables between healthy controls and hypothyroid patient we found prolonged distal onset latency in bilateral median nerve, right ulnar nerve. Along with that, there was prolonged proximal onset latency of left median and tibial nerve in hypothyroid patients (Table 3). Whereas distal onset latency, proximal onset latency, CMAP amplitude, nerve conduction velocity, F wave were not significant in median, ulnar and tibial nerves.

Among heart rate variability measures all the time domain measures (SDNN, RMSSD and PNN50) of HRV were significantly decreased in hypothyroid patients. Similarly, among frequency domain variables (LF, HF, LFnu, HFnu, LF/HF, TP) LF, HF and TP were significantly decreased in hypothyroid patients as compared to healthy control (Table 4).

**Table 4. Comparison of heart rate variability measures between hypothyroid patients and healthy controls.**

| HRV measures | Hypothyroid patients (n = 30); [median(q1-q3)] | Healthy Controls ( n = 30); [median(q1 -q3)] | P value |
|---|---|---|---|
| **Time Domain Measures** | | | |
| SDNN (ms) | 40.3(32.3 - 49.6) | 48.55(37.85 - 60.67) | 0.039 |
| RMSSD (ms) | 31.75(25.1 - 45.25) | 45.5(32.9 - 55.4) | 0.009 |
| PNN50 (%) | 9.8(3.1 - 25.62) | 26.35(12.35 - 39.5) | 0.015 |
| **Frequency Domain Measures** | | | |

| | | | |
|---|---|---|---|
| LF Power ($ms^2$) | 311.5(192.5 - 381.25) | 394.5(249 - 655) | 0.042 |
| HF Power ($ms^2$) | 344(205.75 - 891.25) | 737.5(453 - 1383) | 0.005 |
| LFnu | 38.85(27.4 - 60.875) | 35.5(23.75 - 49.27) | NS |
| HFnu | 61.15(39.12 - 72.6) | 64.5(52.4 - 76.25) | NS |
| LF/HF | 0.63(0.37 - 1.56) | 0.55(0.31 - 0.91) | NS |
| TP ($ms^2$) | 1204.5(791.75 - 1759.5) | 1875(1188.25 - 3591.75) | 0.006 |

*SDNN: Standard deviation of all RR intervals (ms), RMSSD: Root mean square of differences of successive RR intervals (s),PNN50: Percentage of consecutive RR intervals that differ by more than 50 (ms), LF: Low frequency power( $ms^2$), HF: High frequency power( $ms^2$), LFnu: Low frequency normalised units HFnu: High frequency normalised units, TP: Total power, unit of power (ms).*

## DISCUSSION

In present study we found both groups were comparable in term of their age, height, weight, body mass index, upper limb length, lower limb length, pulse rate, systolic blood pressure, diastolic blood pressure.

In sensory NCS; we studied median, ulnar and sural nerves. We found prolonged onset latency, decreased amplitude and conduction velocity only in median nerve in hypothyroid patients as compared to healthy control. Findings are supported by Gupta et al, in which sensory NCS was studied in median and sural nerves in recently diagnosed cases of hypothyroidism. They found prolonged onset in latency, decreased amplitude and conduction velocity both in median and sural nerves.[6] In present study, we found changes in sensory parameters of median nerve only, not in sural and ulnar nerves. It may be because of changes in BMI. In a study done by Gupta et al. BMI of hypothyroid patients was higher than control while in our study BMI of both patients and healthy controls was comparable. As it is known that the deposition of mucopolysachharides leads to compression over peripheral nerves which results in swelling and degeneration in them. One of the factors for causing neuropathy; may be either due to compression of nerve or axonal degeneration or both.

In a study done by Gupta and colleagues, motor NCS was also studied in median, ulnar and tibial nerves. They found increased in latency of median, ulnar and tibial nerves significantly in hypothyroid patients as compared to healthy control. Conduction velocity of all motor nerves and amplitude of median and tibial nerves were significantly decreased in hypothyroid patients as compared to healthy control. They found no significant changes in latency and amplitude of common peroneal and amplitude of ulnar nerve between the groups.[6]

In motor NCS; we studied median, ulnar and tibial nerve and found prolonged onset latency in left and right median nerves, right ulnar and left tibial nerve as compared to the control group. These findings are similar to the study done by Mahadule et al where they assessed motor parameters of NCS in newly diagnosed hypothyroid patients in female and compared with healthy control. They found prolonged in latency, decreased in amplitude, and nerve conduction velocity in median, ulnar and tibial nerves in hypothyroid patients.[7] In our study we found prolonged onset latency in median, ulnar and tibial nerves in hypothyroid patients. There was also decrease in conduction velocity in hypothyroid patients; however, there was no significant difference between control and hypothyroid group. We didn't find change in amplitude in these nerves. In this study also BMI was high in hypothyroid patients while in our study BMI was comparable within the group and this may be the reason we didn't find any change in the amplitude. This was also similar to another study done by Gupta et al.[6]

In present study, we found significant decrease in time domain measures (SDNN, RMSSD and PNN50) and Frequency domain measures (LF Power, HF Power and TP) of HRV in hypothyroid patients in comparison to healthy controls. The time domain measures of HRV; SDNN, RMSSD and PNN50 are markers of parasympathetic modulations (Taskforce, 1996). In frequency domain measures; HF power is a marker of parasympathetic; LF power is a marker of both sympathetic and parasympathetic activity and TP is a marker of overall modulation (Taskforce, 1996).The results, in our study reflects that basically parasympathetic modulation is reduced in hypothyroid patients as compared to healthy control. Mavai and colleagues studied time domain parameters of HRV in 50 hypothyroid, 50 hyperthyroid and 25 healthy controls. They found time domain measures (SDNN, RMSSD and PNN50) significantly reduced in hypothyroid patients as compared to healthy control.[8] Our findings of time domain measures are supported by this study.

In our study, along with time domain measures; frequency domain measures (LF power, HF power and

TP) were also reduced in hypothyroid patient. The result of frequency domain analysis in our study reflects reduced parasympathetic modulation in hypothyroid patients as compared to control. Ahmed and colleagues[9] studied short term HRV on 60 hypothyroid patients, comparing with 30 euthyroid subjects before and after hormone replacement therapy. Data were analysed by power spectral band of HRV and they found TP, LF power, HF power were reduced and LFnu, LF/HF ratio were increased in hypothyroid patients. In our study LF/HF ratio is comparable within the group. Ahmed et al. in their study included female hypothyroid patients whereas in our study both male and female hypothyroid patients were taken. There were changes in the age range and they had studied in female only. This might have affected the study.

One limitation of the study is that it involved one center only, so our interpretation of the results only applies to this study population. So if it would have been done in multiple hospital setting, the better view of nerve conduction and heart rate variability in hypothyroid patients would provide clearer picture of the situation.

## CONCLUSIONS

In present study, both autonomic activity and somatic nerves were affected. In somatic nerves; median, ulnar, tibial and sural nerves were studied and mostly median nerve were found to be affected. In cardiac autonomic activity; parasympathetic activity is more reduced than sympathetic activity.

**Conflict of Interest: None.**

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