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ABSTRACT
Background: Hypothyroidism is a common medical condition in the general population. Usually hypothyroidism has both central and peripheral nerve involvement. The neurologic manifestations occur in conjunction with the systemic features of the disease and may be noted only incidentally. The peripheral neuropathy can be assessed using the sensory motor nerve conduction studies, which is a non-invasive method. Visual Evoked Potentials (VEPs) are electrical potential differences recorded from the scalp in response to visual stimuli. Aim: To study the motor and sensory nerve conduction in the Median nerve and Visual Evoked Potential in the newly diagnosed hypothyroid females. Materials and methods: The sample size is 30. The study design is a cross sectional study. Sensorimotor nerve conduction of the Median nerve and the VEP was done using NUROSTIM NS2 machine, in the department of Physiology, Meenakshi Medical College, Hospital & Research Institute. The statistical analysis was done by Student unpaired t’ test using SPSS software 17 version. Results: There was a significant in the nerve conduction of both motor and sensory components of the cases when compared to the controls. There was statistically significant prolongation of latency P 100 wave of VEP in the study group compared to the control group. Conclusion: Both peripheral and central nervous system are affected in hypothyroidism. To conclude, electrophysiological studies can be useful in the diagnosis of asymptomatic poly neuropathy in hypothyroid patients.

INTRODUCTION
Hypothyroidism is a common medical condition in the general population. The variety of end-organ effects and wide range of disease severity from entirely asymptomatic individuals to patients in coma with multisystem failure can make hypothyroidism an elusive clinical entity. The thyroid hormone is a key regulator of Cellular metabolism in our body. 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 foetal and neonatal life[1]. Usually hypothyroidism has both central and peripheral nerve involvement. The prevalence of neuromuscular disorders related to thyroid dysfunction has been reported to be between 20-80%[2]. This peripheral polyneuropathy, a progressive nerve disorder, to become chronic disability may be due to the defect in axons, nerve cell body or myelin sheath. The neurologic manifestations occur in conjunction with the systemic features of the disease and may be noted only incidentally. However, symptoms and signs of neurologic dysfunction may be the presenting feature in some patients and can contribute significantly to disability. The peripheral neuropathy can be assessed using the sensory motor nerve conduction studies, which is a non-invasive method. Hypothyroidism has been reported to affect both the electroencephalogram (EEG) and the visual evoked potential (VEP) to flash. Stimulation[3]. Visual Evoked Potentials (VEPs) are electrical potential differences recorded from the scalp in response to visual stimuli.

Aim and Objective: To study the motor and sensory nerve conduction in the Median nerve and Visual Evoked Potential in the newly diagnosed hypothyroid females.

MATERIALS AND METHODS
A Prospective study was performed at our institute over a duration of six months.
Study design: Case control study
Control group: 30 healthy euthyroid females in the age group of 20 – 50 years were chosen from the Master Health Check Up.
Study group: 30 newly diagnosed hypothyroid females from the Medicine OPD.
Inclusion Criteria:
- TSH more than 4.5µU/mL or free T4 less than 0.7ng/dL.
- Non pregnant females
- Age between 20 to 50 years
Exclusion Criteria:
- Chronically ill
- Patients on thyroxine treatment
- Subjects with systemic diseases like Diabetes mellitus, Hypertension.
- Chronic associated disorders and other demyelinating neuromuscular disorders.
- Drug induced neuropathy

The present study was conducted in the department of Physiology, Meenakshi medical college, Hospital &
Research institute. The institute ethical clearance was obtained. After getting informed and written consent, history taking and examination were performed. Nerve Conduction Study was performed by using the Standard Neurostim – NS2 machine[6]. The latency, amplitude, duration, area and velocity of motor and sensory component of the Median nerve were studied on both the upper limbs. Three surface disc electrodes, Recording electrode, Reference electrode, Ground electrode were placed after applying jelly to reduce resistance in air between electrode and skin surface. Motor nerve conduction velocity (MNCV) was evaluated by Belly Tendon montage. Sensory nerve conduction velocity (SNCV) was measured by anti-dromic stimulation.

For recording the VEP, the research room was made quiet and comfort and uniform temperature maintained. The subjects were being instructed to fix their gaze at the centre of the checker board, a red square to avoid interference of movement of eyeball. Prior to commencement of the test, the subject is pre adapted to the luminance of the blank screen for five minutes. This was the only source of illumination in an otherwise darkened room. The other eye is covered with opaque material that does not allow light. The function of central visual pathway was evaluated by pattern VEP[5].

The usual spectacles (if any) were allowed to wear during the test. The automatic artifact rejection was used. The electrical activity has low cut of 2 Hertz and high cut of 0.3 Kilo Hertz filters. The disc surface electrodes were used. The sweep speed was 50 ms/division. Then mono ocular stimulation was chosen with flash checker board. The checker board stimulus was produced by a video pattern generator on a computer monitor provided with the polirite, with black and white checks that changed phase abruptly and repeatedly. The luminance modulation of the pattern was selected to give the reversal mode of stimulation at a rate of 2 per second. The check size was 8 x 8 and the monitor 16” x 14”. The luminances of bright and dark checks were adjusted to be 80%. The black and white monitor was placed 100 cm from the study subjects. The signals were amplified, averaged and displayed on the monitor as a waveform. The signal is amplified 50,000 times and band pass filtered between 1 - 300 Hz[6].

**Statistical analysis:** The parameters were analysed by statistical tests – “t” test and Pearson Correlation using SPSS software version 17.

**RESULTS**

In Table I, there is a significant increase in weight and BMI in hypothyroid females (p<0.001) compared to euthyroid females. Table II showed significant decrease in the amplitude and conduction velocity of median nerve (motor) in Hypothyroid. In Table III, sensory nerve conduction in Median Nerve showed significant increase in latency and significant decrease in the conduction velocity and amplitude in the hypothyroid compared to healthy females. In Table 4 the P 100 wave form latency of the cases are significantly prolonged than the controls.

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**Table 1: Comparison of Baseline Characteristics**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Hypothyroid</th>
<th>p VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI in kg/m²</td>
<td>23.6±5.3</td>
<td>26.7±4.94</td>
<td>&lt; 0.01**</td>
</tr>
<tr>
<td>WEIGHT(kgs)</td>
<td>55.44±9.3</td>
<td>63.52±10.77</td>
<td>&lt; 0.01**</td>
</tr>
<tr>
<td>HEIGHT(cms)</td>
<td>152.8±4.84</td>
<td>156.34±5.08</td>
<td>0.08</td>
</tr>
<tr>
<td>AGE in years</td>
<td>35.8±10.80</td>
<td>31.04±9.77</td>
<td>0.09</td>
</tr>
</tbody>
</table>

*p< 0.05 - significant **p<0.01 – Highly significant

**Table 2: Comparison of Motor Nerve Conduction between Hypothyroid And Control Females**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Hypothyroid</th>
<th>p VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency(s)</td>
<td>2.23±0.6</td>
<td>2.6±0.4</td>
<td>0.19</td>
</tr>
<tr>
<td>Amplitude(mv)</td>
<td>12.38±6.7</td>
<td>10.56±2.8</td>
<td>0.03*</td>
</tr>
<tr>
<td>Conduction velocity(M/s)</td>
<td>58.55±6.1</td>
<td>54.26±4.95</td>
<td>0.004**</td>
</tr>
</tbody>
</table>

*p< 0.05 - significant **p<0.01 – Highly significant

**Table 3: Comparison Of Sensory Nerve Conduction Between Hypothyroid And Control Females**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Hypothyroid</th>
<th>p VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency(s)</td>
<td>2.91±0.4</td>
<td>3.48±0.3</td>
<td>0.02**</td>
</tr>
<tr>
<td>Amplitude(mv)</td>
<td>10.92±2.31</td>
<td>7.6±2.9</td>
<td>0.001**</td>
</tr>
<tr>
<td>Conduction velocity(M/s)</td>
<td>58.56±4.15</td>
<td>50.55±7.63</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

*p< 0.05 - significant **p<0.01 – Highly significant

**Table 4: Comparison of wave latency P 100 between hypothyroid females and control females**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Hypothyroid</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left eye</td>
<td>95.68±68</td>
<td>104.44±2.28</td>
<td>0.002**</td>
</tr>
<tr>
<td>Right eye</td>
<td>92.91±1.2</td>
<td>101.47±1.39</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

*p< 0.05 - significant **p<0.01 – Highly significant

**DISCUSSION**

The present study showed that there is subclinical involvement of both peripheral and central nervous system in the newly diagnosed hypothyroid females. The conduction velocity of the motor component of bilateral median nerve of the cases were significantly reduced the latency significantly increased compared to the controls. Our observation is in agreement with the finding recorded by Rao SN et al., 1980 [7] who found abnormal nerve conduction in hypothyroid patients predominantly affecting median and peroneal nerves. They also reported significantly prolonged motor and sensory distal latencies. Sensory nerve Conduction showed an overall decrease in conduction in hypothyroid females compared to control. This decrease is well appreciated and significant in conduction velocity of the sensory component of the median nerve. This also correlated with the study done by Ruud F Duyff et al.,2000 [8] and O Malley et al., 1985 [9]. The thyroid hormone affects the central and peripheral nervous systems via its role in gene expression, production of myelin; it’s effects on the neurotransmitter system and axonal transportation [10].

VEP is simple, non invasive and sensitive technique for evaluating impulse conduction along the optic pathway (central nervous system). It is an effective, simple, non-invasive electro physiological test. In our study the wave latency P 100 was significantly prolonged in the hypothyroid females when compared to the controls. In
our study, a delay in the P100 latencies in hypothyroid groups as compared to the controls was observed. The P100 wave form is generated in the striate and peristriate occipital cortex due to the activation of the primary visual cortex and also due to the discharge of the thalamo cortical fibers. The prolongation of cortical wave latency P100 VEP is simple, non invasive and sensitive technique for evaluating impulse conduction along the optic pathway (central nervous system). It is an effective, simple, non invasive electro physiological test. In our study the wave latency P 100 was significantly prolonged in the hypothyroid females when compared to the controls. In our study, a delay in the P100 latencies in hypothyroid groups as compared to the controls was observed. The P100 wave form is generated in the striate and peristriate occipital cortex due to the activation of the primary visual cortex and also due to the discharge of the thalamo cortical fibers. The prolongation of cortical wave latency P 100 in hypothyroid subjects is more significant that, it suggests there is central nervous system involvement. The latency depends on an intact, myelinated nerve as myelin and salutatory conduction are essential for fast action potential propagation in normal subjects. In contrast, the amplitude of the waveform depends primarily on number of axons functioning within the nerve. Slowing of conduction velocity or prolongation of latency usually implies defects in myelination and loss of amplitude due to axonal dysfunction. El Salem K et al., 2006 noticed motor polyneuropathy in 52% of the patients with hypothyroidism. This is coexistent with our reporting. However, they documented primarily demyelinating motor polyneuropathy in the patients. This goes in contrast to our findings as we have found mixed (axonal and demyelinating) polyneuropathy affecting motor nerves. Nemni et al., 1987 proposed that degeneration of peripheral nerve in hypothyroidism is primarily axonal causing axonal polyneuropathy. This is not in agreement with our findings as we observed mixed type of lesion in our cases.

Our findings signify that there is a definite neurological deficit in thyroid deficiency, which can involve the central nervous system at a much earlier stage and increases with an increased duration of the disease. The neuropathy associated with thyroid dysfunction is responsible for myriad of symptoms. However, a suggestion has been made that subclinical involvement occurs always in hypothyroidism. Peripheral and central nervous system alterations in hypothyroidism have shown that central nervous system is more vulnerable to the effects of hypothyroid than peripheral nervous system. Therefore electrophysiological studies were suggested to be performed in hypothyroid subjects early in the course of thyroid deficiency in order to detect nervous system involvement. Thyroid hormone affects myelination. The demyelination results in delay in nerve conduction responsible for prolonged latency P 100. Hyponatremia, a feature of hypothyroidism may also result in disorder of nerve excitability.

The limitation of the present study is it is a cross sectional design, we do not know the exact duration of illness. A follow up study is needed to record VEP after the subjects become euthyroid. Both gender should be included in the future study.

CONCLUSION

Thus, this study concluded that polyneuropathy associated with hypothyroidism was largely of mixed type (axonal as well as demyelinating type).The presence of electrophysiologic abnormality in hypothyroidism suggested that nerve conduction study is of value for the evaluation and early diagnosis of peripheral neuropathy in hypothyroid patients. This study suggests that periodic evaluation of hypothyroid subjects to such test will help in monitoring the progress of neuropathy and earlier detection of nervous system involvement to reduce the morbidity of hypothyroid patients and a special attention to improve their quality of life. To conclude, electrophysiological studies can be useful in the diagnosis of asymptomatic poly neuropathy in hypothyroid patients.

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Conflicts of Interest: None

REFERENCES