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A comparative study on visual evoked potential (VEP) wave P100 latency in hypothyroid and euthyroid individuals

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***Abstract*---**Hypothyroidism is classified as congenital and acquired according to the time of onset. Consequences of thyroid gland dysfunction also depend on the life stage at which they occur. Peripheral and central nervous system dysfunction are important clinical features of congenital as well as acquired hypothyroidism. Although thyroid hormone effects on the brain are most prominent in development, also in adult-acquired hypothyroidism symptoms such as sensory impairments, disagreeable smells and taste, slowness of thought and action, changes of speech, irritability, headaches ,sleep disturbances, confusion up to delusions and Hallucinations, impairments of memory, of vision as well as of hearing frequently occur. The most prominent and first significant clinical symptom to develop in hypothyroidism is a slowing of speech and of visual perception. These findings indicate CNS involvement in

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hypothyroidism. VEP may be a useful test to detect these changes in early stage of disease.

***Keywords*---**comparative study, evoked potential, hypothyroid, euthyroid.

Introduction

Thyroid diseases are among the commonest endocrine disorders worldwide. India too, is no exception. [1] Hypothyroidism is the most prevalent form of thyroid disease. The prevalence of hypothyroidism in the developed world is about 4-5% whereas the prevalence of subclinical hypothyroidism is about 4-15%. In India, the overall prevalence of hypothyroidism in is 10.95% and subclinical hypothyroidism prevalence is 8.02%. [2] Hypothyroidism is classified as congenital and acquired according to the time of onset. Consequences of thyroid gland dysfunction also depend on the life stage at which they occur. Peripheral and central nervous system dysfunction are important clinical features of congenital as well as acquired hypothyroidism. [4] Although thyroid hormone effects on the brain are most prominent in development, also in adult-acquired hypothyroidism symptoms such as sensory impairments, disagreeable smells and taste, slowness of thought and action, changes of speech, irritability, headaches ,sleep disturbances, confusion up to delusions and Hallucinations, impairments of memory, of vision as well as of hearing frequently occur. The most prominent and first significant clinical symptom to develop in hypothyroidism is a slowing of speech and of visual perception. [5] While deafness of sensory neural hearing loss is the most common otolaryngological manifestations associated with thyroid dysfunction. Actual incidence of hearing loss in hypothyroidism is uncertain, and it may affect 25% of the patients with acquired hypothyroidism and 35-50% of the patients with congenital hypothyroidism. [6]Evoked potentials (EP) provide a reliable and objective measure of function in related sensory system and tracts. These tests are sufficiently sensitive to detect “silent lesions” i.e., physiological changes that are not accompanied by physical signs or localizing symptoms. Some EP features are reproducible over long time periods and they are also objective in measurement, thus free from the subjectivity inherent in scoring physical examination Abnormalities. [7]

Visual evoked potentials (VEP) are particularly useful in the study of optic neuropathies, damage to the retro-chiasmatic visual pathways as well as demyelinating diseases of the CNS and metabolic disorders with CNS involvement in particular hypo or hyperthyroidism. [7]. Visual Evoked potentials (VEP) measure the time that it takes for a visual stimulus to travel from eye to occipital cortex.[8] Visual Evoked Potentials record the electrical potential differences from the scalp in response to visual stimuli and give information about functional integrity of visual system. [9]There are three types of standardized visual stimuli that are described in standards and guidelines for clinical electrophysiology of vision

2016.these are pattern reversal, pattern onset and flash. In pattern VEP and flash VEP responses are evoked by pattern stimuli and flash stimuli respectively .Checkerboard pattern reversal stimulation is the gold standard. [10] Some recent studies have revealed that there is prolongation of both peripheral and central conduction time in hypothyroidism; while other studies suggest that changes in VEPs are not statistically significant. [11].

Rationale

Evoked potentials are particularly suited for a non invasive evaluation of a number of afferent pathways in the nervous system. There is dearth of literature on cognitive function evaluation with Visual evoked potentials (VEP) in hypothyroid patients especially in central part of India. Thus present study was undertaken to assess the functional integrity of optic pathways using Visual evoked potential parameters among hypothyroid patients.

Objectives

- To compare VEP wave P 100 latency in hypothyroid and euthyroid groups.
- To find out correlation between VEP wave P 100 latency and thyroid hormones profile of hypothyroid cases.

Materials and Methods

Study place

- Electrophysiology Lab, Department of Physiology at NSCB, Medical College & hospital, Jabalpur (M.P.)

Study period

- January 2020 to Dec. 2020

Study design

- Comparative cross sectional study.

Study participants

Patients of hypothyroidism (TSH>5.5μIU/ml) who were attending OPD of NSCB Medical College hospital whereasapparently healthy volunteers (preferably attendants/ employees/students/other patients) were taken as comparisongroup for the study.

Inclusion criteria

- Group-1(Hypothyroid Cases)-

- Patient had biochemical evidence of hypothyroidism (TSH>5.5μIU/ml) (both sub-clinical and overt/clinical). Person of both Gender (Male & female) Age between 18 to 50 years.
- Comparison Group (Euthyroid persons)-2
  Apparently healthyage and sex matched volunteers who were not having history of thyroid disease& biochemical evidence of thyroid dysfunction were enrolled for comparison.

Exclusion criteria

- Person with DM, Hypertension, any neurological disorders including peripheral neuropathy & Demyelinating diseases.
- Person with optic neuritis/ optic atrophy, glaucoma, Cataract, vitreous opacities.
- Person suffering from hearing loss and obvious disease of the ears.
- Pregnant women
- Person not willing to participate in the study.

Sample size

40 hypothyroid and 40 euthyroid participants were recruited in the present study. Sample size was calculated using OpenEpi statistical software (version3.01) with 95% confidence Level, 80% Power, 1:1 ratio of cases & control with mean value of 1.74(±0.37) &1.55 (±0.16), based on a study carried out by Sharma K. et al. [12]A total of 36 patients in each group were required. We expected 10% non responders thus in each group 40 patients were recruited.

Sampling method

 Consecutive sampling

Study variables

Age, Sex. Height, Weight, BMI and thyroid hormones levels along with VEP Wave P100Latency.

Study tools

- A predesigned and pretested questionnaire RMS (Aleron series) EMG NCV EP machine
- Automatic BP instrument (Omran)
- Snellen's chart and Tunning fork (512 Hz),
- Weighing Machine & Stadiometer

Study techniques

- Personal interview
- Measurements of anthropometric parameters (age, ht, wt, BMI)

- Thyroid hormones profile
- Clinical examination (including test for visual acuity &Rinne's and weber'**s**tests).
- Recording of VEP (Pattern reversal) wave P100 latency in both Eyes of each participant.

Procedure of Visual evoked potential (VEP) recording

VEP was performed on RMS EMG NCV EP machine in a specially equipped electro-diagnostic room, made dark and sound attenuated for the test.Subjects were seated comfortably about 90 cm away from a video-monitor. The videomonitor was present a black and white checker-board pattern with a fixation spot in the centre of the screen. VEP was recorded using a pattern reversing black and white checkerboard. Pattern reversal stimulus consists of black and white checks that can change phase (black to white and white to black) abruptly and repeatedly at specified number of reversals per second.

The normal recording of pattern-reversal VEP consists of 3waves - N75, P100, and N145. The wave latency P100 which is the most significant parameter was measured from the waveforms recorded.[13]. The volume conducted evoked responses were picked up from scalp using disc type of AgCl electrodes. Standard disc surface electrodes were placed according to the international 10/20 system of electrode placement, with active electrode was placed at Oz approximately 2 cm above the inion , reference electrode at Fz or 12 cm above the inion and ground electrode at the middle of forehead.

Data analysis

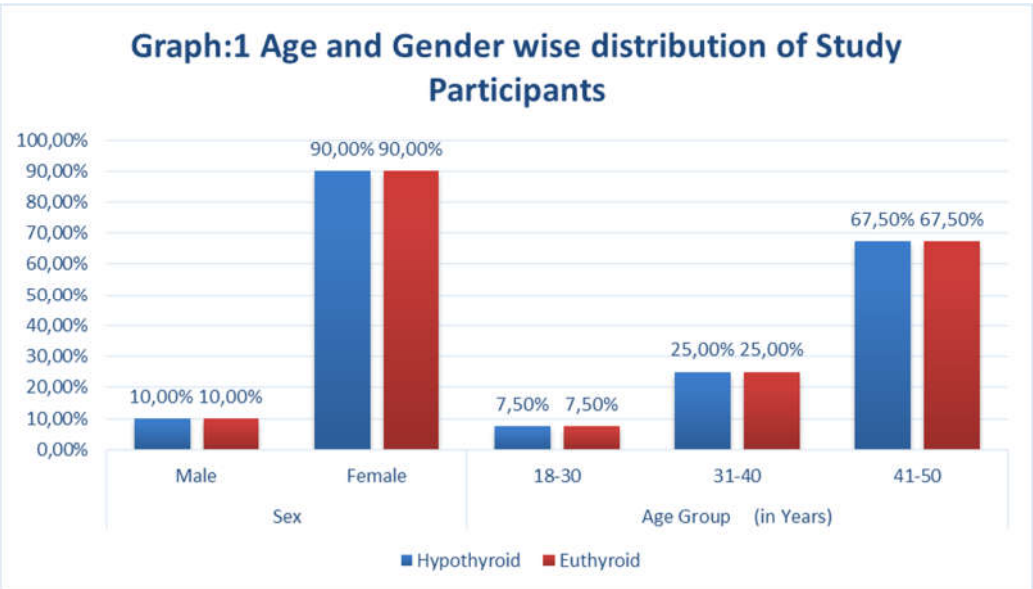
The collected data was compiled and analysed by using:

- MS office-Excel and
- Statistical package for Social Sciences (SPSS-24.0)
- The Quantitative data were expressed as mean± SD
- Unpaired t test was applied to compare quantitative data of the study groups
- Pearson's correlation coefficient was used to find out the association between P 100 latency and thyroid hormones levels.
- p value of less than 0.05 was considered as statistically significant.

Ethical issues

- Ethical clearance from the IEC was obtained.
- Written Informed Consent of all study participants was also taken.

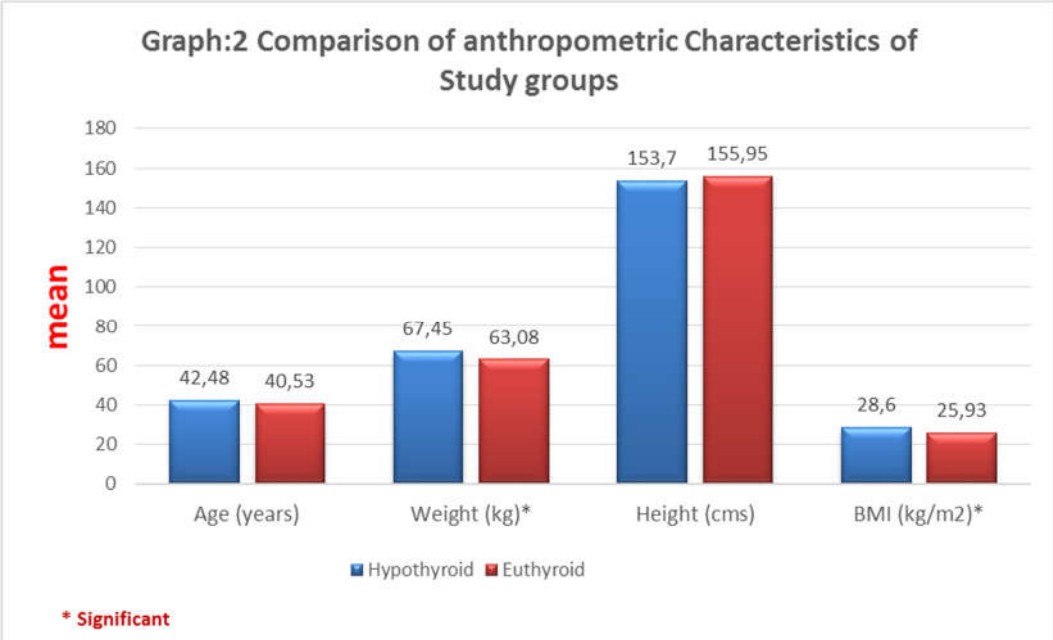
Results



Out of total, 90% study participants were females and 10% were males in both study groups. Maximum (67.5%) of study participants were found to be in the age group of 41-50 years and minimum 3 (7.5%) were in the age group of 18-30 years in both the study groups. Similarly, other studies conducted by Unnikrishnan AG et al [1]also reported higher prevalence of hypothyroidism in females than males and in age group of 46-54 years (13.1%).

Table 2
Comparison of anthropometric Characteristics of Study groups

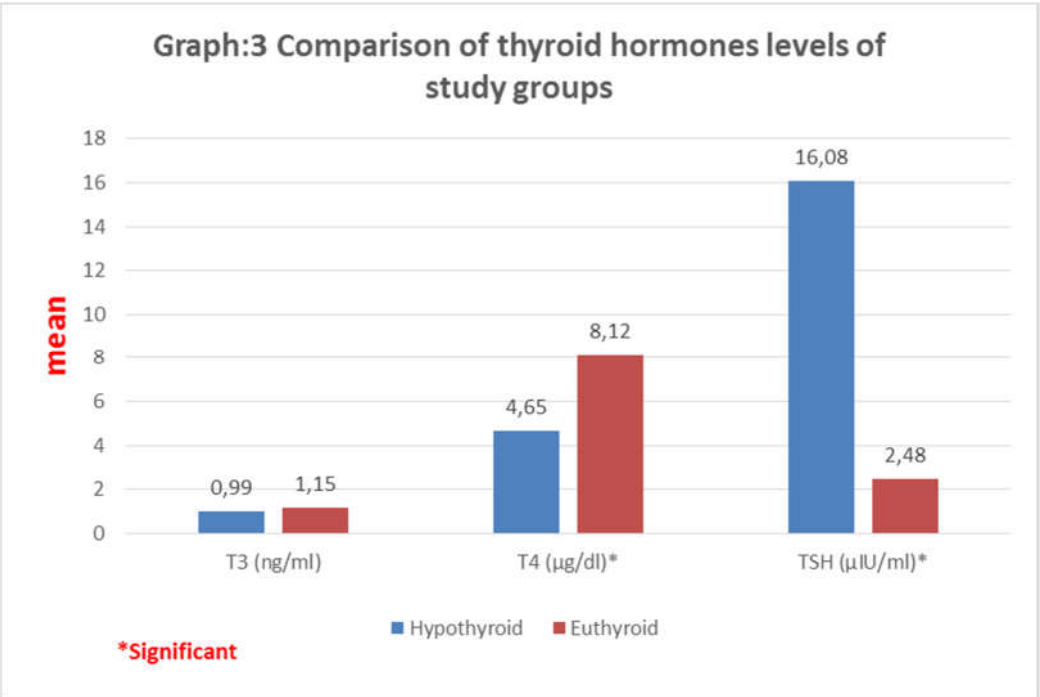
Variables	Hypothyroid (n=40)	Euthyroid (n=40)	t Value	P value
	Mean ± SD	Mean ± SD		
Age (years)	42.48 ± 6.91	40.53 ± 6.74	1.27	0.205
Weight (kg)	67.45 ± 10.38	63.08 ± 8.31	2.08	0.041*
Height (cms)	153.7 ± 6.26	155.95 ± 4.93	1.78	0.078
BMI (kg/m2)	28.60 ± 4.61	25.93 ± 3.17	3.03	0.003*



The mean age (± SD) of hypothyroid individuals was observed as 42.48 (± 6.91) years while that of Euthyroid participants was 40.53 (± 6.74) years. The mean Body mass index (BMI) in hypothyroid group was 28.60 ± 4.61 while it was 25.93 ± 3.17 in Euthyroid group. The difference was also found statistically significant (<0.05). Almost similar mean age of study subjects was observed by B. Nazliel et al [6] andUnnikrishnan AG et al [2] But Gautam V et al [7] reported lower mean age. Several other authors also reported higher BMI in hypothyroid patientsas compared to euthyroid controls.[16,17,18]

Table 3
Comparison of thyroid hormones Profile between hypothyroid and Euthyroid study groups

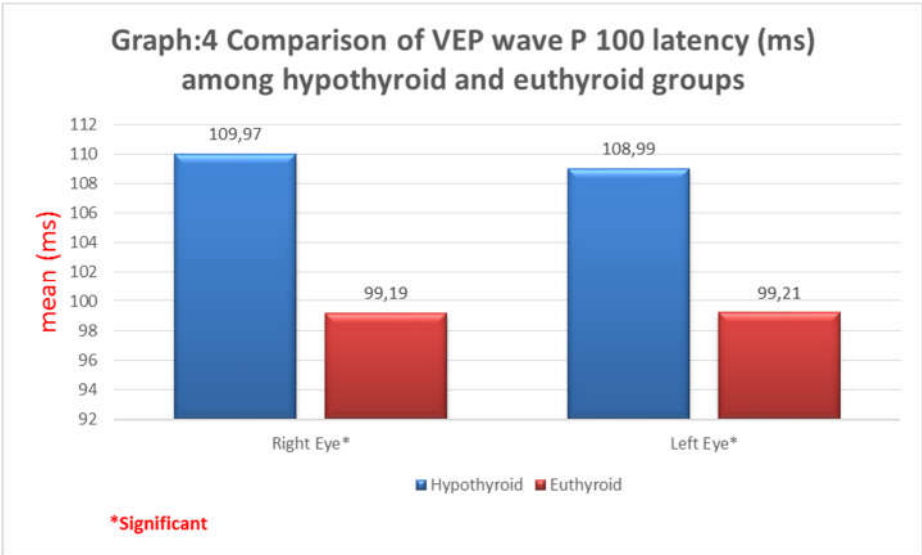
Thyroid hormones	Hypothyroid (n=40)	Euthyroid (n=40)	t Value	p value
	Mean ± SD	Mean ± SD		
T3 (ng/ml)	0.99 ± 0.47	1.15 ± 0.42	1.66	0.10
T4 (µg/dl)	4.65 ± 2.62	8.12 ± 2.14	6.50	0.001*
TSH (µIU/ml)	16.08 ± 13.68	2.48 ± 0.85	9.67	0.001*



Significantly higher level of TSH and lower level of T4 and T3 hormones was noted in hypothyroid group as compared to euthyroid group. These findings of present study are in accordance with the studies done by Paladugu S et al. (2015)[18] and Sharma K et al. (2014) [12]

Table 4
Comparison of VEP wave P 100 Latency (ms) between hypothyroid and Euthyroid group

VEP P100 Latency	Hypothyroid (n=40)	Euthyroid (n=40)	t Value	p value
	Mean ± SD	Mean ± SD		
Right Eye	109.97 ± 5.31	99.19 ± 3.04	11.12	0.001*
Left Eye	108.99 ± 5.60	99.21 ± 3.07	9.67	0.001*



The mean (± SD) values of P 100 latency in right eye of Hypothyroid and Euthyroid groups were 109.97 ± 5.31 and 99.19 ± 3.04 respectively. Whereas the mean values of P 100 latency in left eye of hypothyroid and Euthyroid study group were 108.99 ± 5.60 and 99.21 ± 3.07 respectively. There was statistically significant prolongation of P100 latency in both eyes of hypothyroid patients as compared to Euthyroid participants (P value < 0.05). Similar to observations of the present study, several other studies conducted by Gautam V et al. (2019)[7] Gupta N et al (2016),[14]Khedr EM et al,[15]also revealed significant prolongation of P100 latency in hypothyroid patients as compared to Euthyroid controls.

They opined that thyroid hormones have been shown to affect myelin synthesis, which is an important factor in determining the speed of impulse transmission along complex polysynaptic pathways such as those mediating the visual evoked potentials. However, hypothyroidismcauses central retinal dysfunction and hormonal imbalance that leads tostructural and metabolic alterations which ultimately leads to segmentaldemyelination.Slowing of the conduction velocity or the prolongation of latency usually implies defects in myelination. In hypothyroidism, the mitochondrial oxidative activity,synthesis, degradation of proteins, and sensitivity of tissues to catecholaminesare also affected. Hence demyelination occurs due to the oxidative damage tomyelin membrane and oligodendroglial cell.**[19, 20]**.

Table 7
Correlation between thyroid hormones levels and VEP P 100 latencies in Hypothyroid Group

VEP -100 Latencies	T3 (ng/ml)		T4 (µg/dl)		TSH (µIU/ml)	
	Correlation [r]	p value	Correlation [r]	p value	Correlation [r]	p value
Left Eye	0.026	0.875	-0.099	0.543	0.041	0.802
Right Eye	-0.058	0.724	-0.198	0.724	0.055	0.734

Above table shows that there was a mild positive correlation of P 100 latency with TSH level and a mild negative correlation with T4 hormones level. However, the correlation between thyroid hormones levels and VEP wave P100 latency was not found statistically significant in both Eyes of hypothyroid individuals (p value> 0.05). Similar to our study Khedr EM et al,[15] in their study titled "Peripheral and central nervous system alterations in hypothyroidism: electrophysiological findings", revealed significant prolongation of VEP P100 latency in hypothyroid cases. However there was no significant correlation between thyroid hormones levels and different electrophysiological parameters. Another study by Prosol MW et al.[54]showed significant prolongation of VEP P100 latency in hypothyroid patients than controls but they did not found any significant correlation between P100 latency and thyroid profile. These findings are consistent with our observations. These observations are consistent with the present study.

Conclusion

These findings indicate CNS involvement in hypothyroidism. VEP may be a useful test to detect these changes in early stage of disease.

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