

A COMPARATIVE STUDY OF AUDITORY BRAIN STEM EVOKED RESPONSE IN HYPOTHYROID PATIENTS AND HEALTHY INDIVIDUALS

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Abstract

Background: Thyroid hormone enhances wakefulness, response to various stimuli like auditory sensation, learning and memory capacity. By enhancing gene expression, it influences the synthesis of myelin. The purpose of the study is to assess the auditory pathway with the help of auditory brainstem response (ABR) for risk assessment in hypothyroid patients so as to promote early detection and possible prevention of hearing impairment. **Materials & Methods:** This is a cross sectional study done on 100 subjects of 20 - 50 years in the Research laboratory of Department of Physiology, S.M.S Medical College, Jaipur during period extended from May 2021 to December 2022. The BAER was recorded by using RMS EMG 2000 system with installed BAER software. Two or three trials were performed in order to demonstrate the consistency of the wave form. The absolute latencies of all BAER waves and their IPL of I-III, III-V and I-V were marked with the help of digital cursors and the values were noted down. **Results:** The mean age was 38.32 years for newly diagnosed hypothyroid cases and 35.82 years for normal healthy controls. There was no significant difference between the groups, so they were comparable. The mean Body Mass Index of Group A was 24.9 kg and Group B was 22.8 kg. The hypothyroid patients had higher BMI than control group. There were not statistically significant interaural differences of absolute latencies and interpeak latencies in newly diagnosed hypothyroid patients. There was a positive correlation between serum TSH and the BAER parameters and a negative correlation was found with serum free T3, free T4. **Conclusion:** We found a significant prolongation of absolute latencies and inter peak latencies of brainstem auditory evoked responses in newly diagnosed hypothyroid individuals even before the hearing loss overt.

INTRODUCTION

Hypothyroidism is referred to as “Silent Disease” because the early stage of disease is asymptomatic. About 1.6 billion people are at risk of getting thyroid disorders worldwide.^[1] According to National Health and Nutrition Examination Survey III (NHANES) approximately 4- 5% of population in the developed world is suffering from hypothyroidism and about 4 -15% of people by subclinical hypothyroidism.^[2] The most common cause of hypothyroidism is iodine deficiency. In India, hypothyroidism is classified under the group of Iodine Deficient Disorders (IDD).^[3]

Thyroid hormone governs the rate of metabolism of fats, carbohydrates, proteins and also regulates the timing and pace of the CNS development. Thyroid hormone enhances wakefulness, response to various stimuli like auditory sensation, learning and memory capacity.^[4] By enhancing the gene expression it

influences the synthesis of myelin. Myelin synthesis is an important factor determining the speed of impulse transmission along the complex neural pathway which mediates the evoked potentials.^[5] So, thyroid hormone deficiency leads to delayed neuronal conduction along the central nervous system as well as the peripheral nervous system which reduces the perception of all the sensory stimuli.

Hypothyroidism is the most common endocrine disorder worldwide. It is associated with delayed mental processing and prolonged latencies of evoked potentials. Brainstem auditory evoked responses is a simple noninvasive procedure helps to detect the impairment of CNS as well as the auditory pathway. Thyroid hormone has prominent effects on nervous systems through its role in gene expression, myelin production, neurotransmitter release, and axonal transportation. Likewise for the proper development of auditory system, adequate levels of thyroid

hormones are required.^[6] The exact mechanism of thyroid hormone role in the hearing is uncertain, the possible relationship is revealed by recent cellular level and molecular level experimental studies.

About 25 to 30% of the adult hypothyroid patients have hearing loss. In 1948 Means et al stated that hearing loss is one of the troublesome symptoms of hypothyroidism and it may be conductive, sensorineural or mixed hearing loss.^[7] Being a metabolic hormone, thyroid hormone deficiency leads to reduction in the cell energy production, oxygenation and metabolism of all the organs including inner ear structures like stria vascularis and the organ of corti.^[8]

Thyroid hormone deficiency produces delay in the impulse transmission which leads to alterations in hearing threshold. All these neurological complications of hypothyroidism will resolve completely with thyroid hormone replacement especially when diagnosed at the early stage.^[9]

Hearing loss in infants and children due to congenital hypothyroidism results in serious impairment in language, communication skills, cognitive and emotional development. In adults hearing loss will lead to loneliness, social isolation, psychiatric disturbances, depression, occupational stress and relatively low earnings.^[10] There are literatures pointing out that early treatment of hypothyroidism will reverse the hearing loss.^[11,12]

Now a days Brainstem Auditory Evoked Response (BAER) is mainly used for screening the preterm infants and also prior to cochlear implantation. The BAER recording for finding the functional integrity of auditory pathway is rarely performed in hypothyroid patients in neurology and otolaryngology practice. The findings of various studies stated that the delay in the auditory processing time may provide information about the subclinical involvement of central as well as peripheral neuropathy in hypothyroid individuals. So, BAER can be used as a screening test to find the central nervous system involvement and the hearing loss in hypothyroid patients even in the earlier stage itself. The purpose of the study was to assess the auditory pathway with the help of auditory brainstem response (ABR) for risk assessment in hypothyroid patients so as to promote early detection and possible prevention of hearing impairment.

MATERIALS AND METHODS

This is a cross sectional study done on 100 subjects of 20 - 50 years in the Research laboratory of Department of Physiology, S.M.S Medical College, Jaipur during period extended from May 2021 to December 2022.

The ethical committee of the SMS Medical College approval was obtained prior to the commencement of the study.

Inclusion Criteria

A total of 100 subjects of 20 - 50 years were included in the study. Among them 50 were newly diagnosed

hypothyroidism patients and 50 were normal healthy controls.

Exclusion Criteria

- Known patients of hypothyroidism already on treatment,
- Persons working in noisy environment
- Pregnant females,
- Known cases of any hearing loss,
- Systemic illness like diabetes mellitus, hypertension, collagen disorders and neurodegenerative diseases
- H/o drug intake - ototoxic drugs, anticonvulsant drugs, anticancer drugs.
- H/o head injury

Case Selection

- Patients who came with the symptoms and signs suggestive of hypothyroidism such as easy fatiguability, dry skin, hoarseness of voice, cold intolerance, weight gain, periorbital swelling and bradycardia were randomly selected from the medicine outpatient department.
- Thyroid profile was done for all of them which include the serum parameters of TSH, free T3, free T4. 50 patients diagnosed as hypothyroidism were selected as study subjects and 50 age matched healthy people with normal thyroid profile were taken as controls.
- They were selected from the general population in Jaipur. None of the cases and controls had any symptoms and signs of CNS dysfunction and none of them showed any abnormality in neurologic examination and were not on treatment with thyroxine.

Hormone Measurement

Thyroid profile includes serum TSH, free T4, free T3 and they measured by microplate-based Enzyme Linked Immuno Sorbent Assay (ELISA) using ERBA kit. This method is based on one step immune enzymatic principle associated with the Biotin – Streptavidin Technology. The reference values are,

- TSH – 0.4 to 5.5 μ IU/ml
- FreeT3 – 1.4 to 4.2 pg/ml
- FreeT4 – 0.8 to 4.2 ng/ml

Procedure for recording Brainstem Auditory Evoked Potentials

The BAER was recorded by using RMS EMG 2000 system with installed BAER software. The subjects were asked to sit comfortably in a fully relaxed state and with eyes closed. The skin at the site of placement of surface electrode was cleaned with spirit and the electrodes were placed on the scalp, according to the 10 - 20 International System using EEG paste.

The site of placement of electrodes:

- Active electrode on the Vertex (Cz)
- Reference electrodes over the Right and Left mastoid process
- Ground electrode on the forearm

BAER Recording Technique

The guidelines for clinical and intraoperative recordings of BAER was proposed by American

clinical neurophysiology society, 2006 and American Electroencephalographic society 1994 respectively.^[13] The BAER amplitudes are in the sub microvolt range. It is much weaker than the surrounding environmental noise, background electro cerebral activity and muscle activity. Hence BAER recordings require special amplifiers called bio amplifier to make these signals large enough for further signal processing, filters for filtering the undesirable electrical activity, digital converter for converting the scalp recorded electrical activity to binary format that can be utilized by a digital computer and a signal averager.^[14]

Stimulus

A mixed frequency of broad band clicks (100 to 8000Hz), using the acoustic energy over a wide range of audio frequencies can be used for the neurologic evaluation. Clicks are single monophasic square wave pulse delivering for 100µsec duration by using a standard audiometric ear speaker. These clicks stimulates a large number of neurons which fired simultaneously and produce a larger response.^{13,15}

Stimulus polarity

Based on the type of pressure applied to the tympanic membrane three types of stimulus polarities are present. They are,

- Rarefaction click
- Condensation click
- Alternating polarity

The clicks in which first and most prominent acoustic wave creates a positive pressure and displays the tympanic membrane outwardly is referred to as rarefaction clicks. The clicks in which the acoustic wave creates a negative pressure and displays the tympanic membrane inwardly are called as condensation clicks. Alternating polarity is the clicks

which creates alternating negative and positive pressure and displaces the tympanic membrane inwardly and outwardly.

In this study rarefaction type of stimuli is used, because it will produce better resolution of the BAER waves. The filter frequency was set between 100 to 3000 Hz, analysis time 10ms and sensitivity 1µV/division. A total of 2000 stimuli at the frequency of 10Hz were delivered to the testing ear within 0.1ms.

The intensity of stimulus was 60dB above the sound pressure level. To the contralateral ear 40dB white noise was given for masking. Two or three trials were performed in order to demonstrate the consistency of the wave form. The absolute latencies of all BAER waves and their IPL of I-III, III-V and I-V were marked with the help of digital cursors and the values were noted down.

RESULT

The mean age was 38.32 years for newly diagnosed hypothyroid cases and 35.82 years for normal healthy controls. There was no significant difference between the groups, so they were comparable. The mean Body Mass Index of Group A was 24.9 kg and Group B was 22.8 kg. The hypothyroid patients had higher BMI than control group (table 1). There are not statistically significant interaural differences of absolute latencies and interpeak latencies in newly diagnosed hypothyroid patients (table 2). There was a positive correlation between serum TSH and the BAER parameters and a negative correlation was found with serum free T3, free T4 (table 3).

Table 1: Demographic characteristics of Study Population

Variables	Group A	Group B
Participants	50	50
Mean Age	38.32	35.82
Mean Height (CM)	153.8	155.04
Mean Weight (Kg)	59.04	54.84
BMI (mean)	24.9	22.8

Table 2: Interaural differences of Latencies and interpeak latencies in newly diagnosed in Hypothyroid patients

WAVES	Right Ear		Left Ear		P value
	Mean	SD	Mean	SD	
I	1.68	0.12	1.71	0.15	0.11
III	3.67	0.16	3.62	0.15	0.11
IV	4.84	0.2	4.85	0.17	0.1
V	5.63	0.23	5.6	0.28	0.1
I-III	2.94	0.83	1.9	0.2	0.0001
III-V	5.2	0.76	3.89	0.35	0.001
I-V	2.38	0.76	2.4	0.71	0.1

Table 3: Correlation between TSH, T3 & T4 and latencies and interpeak Latencies

Correlation with	Correlation coefficient (r)		
	TSH	T3	T4
Right ear Latencies			
I	0.60	-0.53	-0.56
III	0.54	-0.38	-0.45
V	0.39	-0.31	-0.3
Left ear Latencies			

I	0.56	-0.39	-0.46
III	0.47	-0.26	-0.3
V	0.25	-0.1	-0.16
Right ear Interpeak latencies			
I-III	0.32	-0.25	-0.23
III-V	0.12	-0.03	-0.03
I-V	0.24	-0.15	-0.27
Left ear Interpeak Latencies			
I-III	0.34	-0.14	-0.24
III-V	0.07	-0.12	-0.02
I-V	0.27	-0.12	-0.28

DISCUSSION

Central nervous system dysfunctions are the important consequences of hypothyroidism. It is associated with motor deficits, hearing impairment, mental retardation, depression and memory deficit. The most common otolaryngological manifestation of hypothyroidism is hearing impairment.^[8] It may be conductive, sensorineural or mixed type of hearing loss. Parving et al^[16] in 1983 and Isam et al in 2001^[17] were reported in their study that SNHL was the predominant type of hearing loss in hypothyroid people. Early treatment of hypothyroidism with thyroid hormone will completely revert the hearing impairment.^[8] Intact anatomical pathway, relay stations and proper myelination of nerves are some of the factors that determine the functional ability of the auditory pathway.^[12] The absolute and inter peak latencies in BAER recordings denote the conduction of nerve impulses along the different segments of the auditory pathway and it also can be used as a tool to assess the hearing impairment.

The present study deals with the BAER changes in newly diagnosed hypothyroid individuals. The Absolute and interpeak latencies were recorded and analyzed between newly diagnosed hypothyroid individuals and healthy controls. Various electrophysiological studies provide an almost unanimous opinion that thyroid hormone substitution promotes complete reversal of hearing loss.^[10,11] Therefore to make sure that the changes in the BAER parameters are exclusively due to thyroid hormone deficiency, only the newly diagnosed hypothyroid cases were selected in this study.

In the present study 50 newly diagnosed hypothyroid cases of mean age 38.32 years and normal healthy controls of mean age 35.82 years were included. About 70% of the newly diagnosed hypothyroid cases were predominantly in the age group of 35 to 45 years. It is consistent with the report of myxedema committee in London which said that middle aged women were mostly affected by hypothyroidism than men.^[18] The BAER are far field subcortical electrical potentials which helps to assess the auditory sensory process from distal part of the cochlear nerve to the brainstem.^[19,20] So in this study the BAER was recorded among newly diagnosed Hypothyroid cases and healthy controls and found that there was statistically significant ($p < 0.0001$) increase in absolute latencies of wave I, III, IV and V in newly diagnosed hypothyroid cases. Similarly, interpeak

latencies I - III, III-V and I-V were also prolonged significantly ($p < 0.0001$) in them compared to controls. This was consistent with the study results of other researchers.^[21,22]

In 1981 Himelfarb et al^[23] in their study on Auditory brainstem responses in thyroid disorders inferred that the changes in the BAER pattern were characterized by prolonged brainstem conduction time, flattened peaks and diminished amplitude. Another study done by CL Lai from Taiwan analyzed the brainstem auditory evoked responses from 20 patients of primary hypothyroidism, observed that the peak and interpeak latencies were delayed significantly in them.^[24]

Anjana et al in their evoked potential study found a delayed conduction of impulses along the superior olivary nucleus which leads increased wave III latency but did not find any significant difference in other absolute and IPL of hypothyroid individuals. They found significant improvement in wave III conduction time and IPL of I -III after thyroid hormone therapy. By this study they proposed that optimal thyroid hormone level is required to improve the excitability of neuronal generators in the brainstem auditory pathway particularly for wave III and V.^[12]

In our study there was a significant increase in the absolute latencies of wave forms I, III, IV and V was observed. Similar to the present study results, Thornton and Jarvis from MRC institute of hearing research, UK^[25], Santos et al^[8], Khedr et al^[26] and Hohmanet al^[27] also showed increase in the wave latencies. They suggested that this may be due to slow conduction of nerve impulses along the auditory pathway. Because the BAER wave latencies depend on the functional integrity and myelination of the auditory pathway.^[10]

Hypothyroidism being a metabolic disorder it affects the oxidative activity of mitochondria, lipid level in the CNS, protein synthesis and degradation which leads to demyelination.^[8] The increased absolute latency of I, III and V in this study indicates that the thyroid hormone deficiency affects the myelination of both peripheral and central part of the auditory pathway. It was further supported by the molecular level experimental studies.

Moore et al^[28] and Knipper et al^[29] inferred that thyroid hormone is essential for the expression of myelin genes like peripheral protein zero (P0), major basic protein (MBP) and proteo lipid protein (PLP) in cochlea, brainstem and auditory cortex. So thyroid

hormone deficiency will lead to hypomyelination of the peripheral and central part of the intradural segment of the auditory nerve and produces enhanced wave latencies.

In 1983 Abbott et al.^[30] said that the prolonged central conduction time of nerve impulse in hypothyroidism may be attributed to low body temperature and altered cerebral metabolism.

In the present study there was a significant prolongation of all IPL observed in newly diagnosed hypothyroid patients. This result was consistent with the results of Anand et al.^[31], Santos et al.^[8] and Khedr et al.^[26]

The overall findings signify that both peripheral and central auditory pathway are affected by hypothyroidism. The proposed possible mechanisms for the hearing loss in hypothyroidism are multifactorial, like defective myelination, reduced body temperature, altered cerebral metabolism, diminished regulatory protein actions, reduced sensitivity of sensory receptors, decreased voltage gated sodium current density and axonal degeneration caused by deposition of glycosaminoglycan.

In contrary to the above studies, some of the researchers have showed disagreeing results in their studies. A study by Vanasse et al done on 15 adult hypothyroid patients of age ranging from 34 to 82 years found no significant differences in BAER before treatment. They stressed that hearing loss in these patients may be due to aging than to hypothyroidism.^[32] Several studies were done to find the normative data of BAER parameters have found that no significant difference existed between the right and left ears.^[10]

In the present study there was a positive correlation of BAER latencies with serum TSH and negative correlation with serum free thyroid hormone levels. This was consistent with the following study results. Himelfarb et al found statistically significant relation between the hearing loss and the serum level of low free T4.^[23] Ben Tovim et al done an experimental study on rats, inferred that the BAER changes are directly associated with the serum level of free T4. This correlation suggests that there is direct involvement of auditory pathway by thyroid hormone deficiency and results in delaying of impulse transmission time in BAER recordings.^[33]

CONCLUSION

We found a significant prolongation of absolute latencies and inter peak latencies of brainstem auditory evoked responses in newly diagnosed hypothyroid individuals even before the hearing loss overt. So, it should be recommended that BAER may be added to the list of screening tools for a more accurate and early assessment of neurological involvement in hypothyroid individuals to initiate treatment to ameliorate symptoms and prevent complications. Because better hearing gives better life promise.

REFERENCES

1. Khan A, Muzaffar AK, Akhtar S. Thyroid disorders, etiology and prevalence. *Journal of Medical Sciences* 2002; 2: 89-94.
2. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, Braverman LE. Serum TSH, T4 and thyroid antibodies the United States Population (1988 to 1994): National Health and Nutrition Examination Survey III (NHANES). *The J Clinical Endocrinology and Metabolism* 2002; 87(2): 489 - 99.
3. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian J Endocrinology and Metabolism* 2013; 17(4): 647- 52.
4. Bruce M Koeppen, Bruce A Stanton. *Berne and Levy Physiology*, 6th edition, Saunders Elsevier, 2009; 8, 41: 138 - 50, 725- 36.
5. Yuksel G, Karlikaya G, Tanridag T, Onder US, Akyuz G. Nerve conduction studies, SEP and Blink reflex studies in recently diagnosed untreated thyroid disease patients. *J Neurol Sci (Turk)* 2007; 24: 7-15.
6. Mescher AL. *Junqueira's - Basic Histology, Text and Atlas*. 12th edition, Mc Graw - Hill, Lange 2010: 363.
7. Howarth AE, Lloyd HED. Perceptive deafness in hypothyroidism. *Deafness in Hypothyroidism, British Medical Journal* 1956; Feb 25: 431 - 2.
8. Santos KTP, Dias N H, Mazeto GM S, Carvalho LR, Lapate RL, Martins RHG. Audiologic evaluation in patients with acquired hypothyroidism. *Braz J of Otorhinolaryngol* 2010; 76(4): 478 -84.
9. Walter G Bradley, Robert B Daroff, Fenichel GM, Jankovic J. *Neurology in Clinical Practice. The neurological disorder*, 5th edition, Volume -2; Butterwork Heinemann Elsevier: 1062- 64.
10. Mathers CD, Smith A, Concha M. Global burden of hearing loss in the year 2000; version 2: 1 - 30.
11. Aggarwal M.K, Bir Singh G, Nag RK, Singh S.K, Rajesh Kumar, Yadav M. Audiological evaluation in Goitrous Hypothyroidism. *International Journal of Otolaryngology and Head & Neck surgery* 2013; 2: 201 - 6.
12. Anjana Y, Vaney N, Tandon O.P., Madhu S.V. Functional status of Auditory pathways in Hypothyroidism: Evoked Potential Study. *Indian J of Physiology Pharmacology*, 2006;50 (4): 341- 9.
13. Walsh P, Kane N, Butler S. The clinical role of evoked potentials. *J Neurol Neurosurg Psychiatry* 2005; 76: 16 - 22.
14. Binne CD, Cooper R, Manguiere F, Osselton JW, Prior PF, Tedman BM. *Clinical Neurophysiology, Reversed and Enlarged Edition. EMG, Nerve conduction and Evoked Potentials*, Elsevier; Volume I: 391 - 422.
15. Moller AR, Burgess J. Neural generators of the BAEP in the rhesus monkey, *Electroencephalogr Clinical Neurophysiol* 1986; 65: 361-72.
16. Parving A, Parving HH, Lyngsoe J. Hearing sensitivity in patients with myxoedema before and after treatment with L-thyroxine. *Acta otolaryngologica* 1983; 95: 315-21.
17. Isam Al Shuraidah M, Saad Shaheen Al-Taher, Mazin H, Al- Hawaz. Deafness in hypothyroidism, an evaluation of 47 patients. *Basrah J Surgery* Sep 2001; 143 - 48.
18. Brandt N, Kuhn S, Munkner S, Braig C, Winter H, Blin N, Vonthein R, Knipper M, Engel J. Thyroid hormone deficiency affects postnatal spiking activity and expression of Ca²⁺ and K⁺ channels in rodent inner hair cells. *The journal of neuroscience*, March 2007; 27 (12): 3174 - 86.
19. Moore JK, Perazzo L M and Braun A. Time course of axonal myelination in the human brainstem auditory pathway. *Hearing Research* 1995; 87: 21-31.
20. Stanley A Gelfrand. *Hearing - An introduction to psychological and physiological acoustics*. Revised and Expanded, 4th edition, Informa health care; chapter 6: 225 - 27.
21. Mahin H, Hovsepian S, Hashemi M, Amini M, Kelishadi R, Sadeghi S. Hearing impairment in congenitally hypothyroid patients. *Iranian J Pediatrics* 2012; 22(1):92 - 96.
22. Bellman SC, Davies A, Fuggle PW, Grant DB, Smith I. Mild impairment of neuro otological function in early

- treated congenital hypothyroidism. Archives of disease in childhood 1996; 74: 215 – 18.
23. Himelfarb MZ, Lakretz T, Gold S, Shanon E. Auditory Brain stem responses in thyroid dysfunction. J Laryngol Otol Jul 1981; 95(7): 679 – 86.
 24. Lai CL, Tai CT, Liu RT, Howng SL. A longitudinal study of central and peripheral nerve conduction in hypothyroid rats. J Neurol Sci 1997; 148: 139-45.
 25. Thorton ARD, Jarvis SJ. Auditory brainstem response findings in hypothyroid and hyperthyroid disease. Clinical Neurophysiology 2008; 119: 786 – 90.
 26. Khedr M E, El Toony F. L, Tarkhan N M, Abdella G. Peripheral and Central Nervous System Alterations in Hypothyroidism: Electrophysiological Findings. Neuropsychobiology, 2000; 41: 81- 94.
 27. Hohmann D, Kahaly G, Warzelhan J. Effect of hyperlipidemia and hypothyroidism on auditory evoked brainstem responses. HNO 1990; 38 (12): 446 – 50.
 28. Moore JK, Perazzo L M and Braun A. Time course of axonal myelination in the human brainstem auditory pathway. Hearing Research 1995; 87: 21-31.
 29. Knipper M, Bandtlow C, Gestwa L, Kopschall I, Rohhcock K, Wiechers B, Zenner H P, Zimmermann U. Thyroid Hormone affects schwann cell and oligodendrocyte gene expression at the glial transition zone of the VIII nerve prior to cochlea function. Development 125, 1998; 3709- 18.
 30. Abbott RJ, Mally BP, Barnett BB, Timson L, Rosenthal FD. Central and Peripheral nerve conduction in thyroid dysfunction - the influence of L- thyroxine therapy compared with warming upon the conduction abnormalities of primary hypothyroidism. Clinical Science 1983; 64: 617.
 31. Anand VT, Mann SB, Dash RJ, Mehra YN. Auditory investigations in hypothyroidism, Acta otolaryngol 1989;108 (1-2): 83 – 87.
 32. Vanasse M, Fischer C, Berthezene F, Roux Y, Volman G, Mornex R. Normal brainstem auditory evoked potentials in adult hypothyroidism. Laryngoscope 1989; 99(3): 302–6.
 33. Ben Tovim R, Zohar Y, Laurian N, Zohar S, Laurian L. Auditory brainstem response in experimentally induced hypothyroidism in albino rats. The Laryngoscope 1985; 95(8): 982 – 86.