Original Article

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Does Acquired Hypothyroidism Affect the Hearing Functions?

Kazanılmış Hipotiroidizm İşitme Fonksiyonlarını Etkiler mi?

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Abstract

Purpose: It is well known that congenital hypothyroidism can cause hearing loss. However, conflicting results were found in studies investigating hearing functions in acquired hypothyroidism. Therefore, we evaluated the audiometric findings in patients with acquired hypothyroidism.
Material and Method: The study included 58 patients with hypothyroidism and age- and gender-matched 34 healthy controls. Twenty eight (48.27%) patients had subclinical hypothyroidism, and 30 (51.73%) had obvious hypothyroidism. All subjects had a normal otoscopic examination and tympanometry. Pure tone audiometry at 250, 500, 1000, 2000, 4000, 6000, and 8000 Hertz (Hz) was performed in both groups. Blood pressure measurements and the levels of plasma electrolytes, lipids and vitamin B12 were available in all subjects.
Results: Hypothyroidism group and control group were similar with respect to systolic and diastolic blood pressures and plasma glucose, lipid, vitamin B12, calcium, sodium, potassium, and chloride levels. Significantly higher audiometric thresholds (dB) at 250 (10 (0-45) vs. 5 (0-15), p<0.001) and 500 Hz (10 (0-40) vs. 10 (-5-15), p=0.003) were recorded in hypothyroid patients compared to that in healthy controls. Hearing thresholds at 250 and 500 Hz correlated positively with thyroid-stimulating hormone (TSH), and negatively with free triiodothyronine and free thyroxine. Subclinical hypothyroid patients had a higher hearing threshold at 250 Hz than healthy controls (p=0.001).
Discussion: Our study demonstrated that hearing ability decreases in hypothyroidism, even in subclinical hypothyroidism. The changes in TSH and thyroid hormone levels seem to be directly related to the hearing loss in this population of patients.
Keywords: Hypothyroidism, hearing function, audiometry

Öz

Amaç: Konjenital hipotiroidizmin işitme kaybına neden olabileceği iyi bilinmektedir. Ancak, kazanılmış hipotiroidizmde işitme fonksiyonlarını araştıran çalışmalarda çelişkili sonuçlar bulunmuştur. Biz kazanılmış hipotiroidisi olan hastaların odyometrik bulgularını inceledik.
Gereç ve Yöntem: Çalışmaya yaş ve cinsiyet dağılımları benzer olan 58 primer hipotiroidili hasta ile 34 sağlıklı kişi alındı. Yirmi sekiz (%48,27) hastada subklinik hipotiroidizm, 30 (%51,73) hastada aşikar hipotiroidizm mevcuttu. Tüm katılımcıların otoskopik ve timpanometrik muayeneleri normaldi. Grupların saf ses odyometride 250, 500, 1000, 2000, 4000, 6000, 8000 Hertz'de (Hz) işitme eşikleri (dB), kan basınçları ve plazma elektrolit, lipit, vitamin B12 düzeyleri değerlendirildi.
Bulgular: Hipotiroidi ve kontrol grupları sistolik ve diastolik kan basıncı, plazma glukoz, lipit, vitamin B12, kalsiyum, sodyum, potasyum ve klor düzeyleri açısından benzerdi. Odiyometride 250 (10 (0-45) ve 5 (0-15), p<0,001) ve 500 (10 (0-40) ve 10 (-5-15), p=0,003) Hz'de işitme eşikleri hipotiroidili hastalarda sağlıklı kontrol grubuna kıyasla istatistiksel anlamlı yüksekti. Korelasyon analizinde 250 ve 500 Hz'de işitme eşiklerinin tiroid uyarıcı hormon (TSH) ile pozitif korelasyon, serbest trliyodotironin ve serbest tiroksin düzeyleri ile negatif korelasyon gösterdiği tespit edildi. Subklinik hipotiroidili hastalarda 250 Hz'de işitme eşiği kontrol grubuna kıyasla istatistiksel anlamlı yüksek bulundu (p=0,001).
Tartışma: Çalışmamız hipotiroidili hastalarda, subklinik hipotiroidizmli olsalar bile, işitme eşiklerinin yükseldiğini yani işitme fonksiyonlarının bozulduğunu ortaya koymuştur. Bu hasta popülasyonunda, TSH ve tiroid hormon düzeylerindeki değişimler işitme azalması ile doğrudan ilişkili görünmektedir.
Anahtar kelimeler: Hipotiroidizm, işitme fonksiyonları, odyometri

Introduction

Thyroid hormone is essential for normal development of auditory system (1). Thyroid hormone deficiency during fetal and early postnatal thyroid hormone-sensitive periods of inner ear development results in various degree of congenital deafness (2). Hearing loss has been reported in 30-50% of patients with congenital hypothyroidism (3). The treatment of thyroid hormone deficiency is recommended to be initiated before the age of one year (4). Thyroid hormones acting through thyroid hormone receptor-ß initiate myelinogenesis of the cochlea and

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vestibulocochlear nerve (5). Additionally, expression of cochlear motor protein prestin, which regulates outer hair cells' functions, has been shown to be reduced in the absence of thyroid hormone (6).

Although the relationship between congenital hypothyroidism and hearing impartment is well established, the results from the audiological evaluation of patients with acquired hypothyroidism are conflicting. Thus, in this study, we assessed the hearing functions in patients with acquired hypothyroidism, using pure tone audiometry.

Materials and Methods

Study Design and Participants

This study was undertaken in the outpatient clinics of the department of endocrinology and the department of otolaryngology at Ankara Numune Research and Training Hospital between January 2011 and February 2012. The protocol was approved by the local ethics committee.

We studied 58 patients with hypothyroidism and 34 age- and gender-matched healthy controls. Out of 58 patients, 28 (48.27%) had subclinical hypothyroidism (elevated thyroid-stimulating hormone (TSH) with normal values of free thyroxine (T4) and free triiodothyronine (T3)) and 30 (51.73%) had obvious hypothyroidism (elevated TSH with low free T4). 74% of patients had hypothyroidism secondary to Hashimoto's thyroiditis, and 26% had hypothyroidism due to previous partial thyroidectomy. All patients had newly diagnosed hypothyroidism, and none of them were receiving thyroid hormone replacement therapy.

Exclusion criteria for both groups were as follows: previous audiological or otological diseases, ototoxic medicine or substance use, acoustic trauma, ear surgery, perforated tympanic membrane, having a conductive hearing loss or type B or C tympanometric curve, history of hereditary hearing loss, a genetic syndrome, central nervous system pathology (cranial trauma, tumor, infection, or radiotherapy), any electrolyte imbalance, vitamin B12 deficiency, hypertension, diabetes mellitus, coagulation disorders, cardiovascular disease, acute/chronic inflammatory/infectious disease, malignancy, renal or hepatic failure, alcohol or cigarette consumption, and/or pregnancy. All subjects had a normal otoscopic examination and a normal (type A) tympanogram.

Audiometry Test

Pure tone audiometry was performed in a sound-proof booth, using an Interacoustic Clinical Audiometer (model AC40; Assens, Denmark). A TDH 39 standard earphone was used for the air-conduction thresholds while bone-conduction vibrators were used for bone-conduction thresholds. Pure tone air-conduction thresholds were determined for each ear at 250, 500, 1000, 2000, 4000, 6000, and 8000 Hertz (Hz). Bone-conduction thresholds were measured at 500, 1000, 2000, and 4000 Hz. Because none of the subjects had air-bone gaps, air-conduction thresholds were used for the hearing assessment in all subjects.

Laboratory Assays

Venous blood samples were obtained for all patients from the antecubital region between 8:00 and 9:00 a.m., after an 8-12 hour overnight fast. Serum TSH (normal range: 0.34-4.25 μIU/ml), free T3 (normal range: 2.5-3.9 pg/ml), and free T4 (normal range: 0.61-1.2 ng/dl) levels were evaluated using the Abbott Architect 2000 device and Chemiluminescence Microparticle Immunoassay (CMIA) method. Anti-Tg (normal range: <115 IU/ml) and anti-TPO (normal range: <9 IU//ml) serum values were evaluated through immunoradiometric assay (IRMA) methods (ICN Pharmaceuticals, USA).

Statistical Analysis

The SPSS for Windows 13.0 package program was used for the statistical analysis of the data. The Kolmogorov-Smirnov test was used to test the normality of the distribution of the measurable parameters. Data were expressed as mean ± standard deviation for normally distributed continuous variables, whereas continuous variables not normally distributed were shown as median (minimum-maximum). When comparing the groups, the Student's t-test was used for the normally distributed subset, and the Mann-Whitney U test was used for the abnormally distributing subset. Chi-square test was applied for comparison of gender differences between hypothyroid group and control group. The Kruskal-Wallis test was used to compare the hearing thresholds among subclinical hypothyroid group, obvious hypothyroid group, and control subjects. When a p-value from the Kruskal-Wallis test statistics was statistically significant, a Mann-Whitney U test with Bonferroni correction was performed to compare the groups two-by-two. Degrees of association between hearing thresholds and clinical and laboratory variables were analyzed using Spearman's correlation test. A p-value of less than 0.05 was considered indicative of statistical significance.

Results

The clinical and laboratory features of the participants are summarized in Table 1. There were no significant differences between hypothyroid patients and healthy controls with regard to age and gender distributions, blood pressure measurements, hemoglobin, white blood cells, sedimentation, vitamin B12, serum electrolytes, and lipid levels.

Hearing thresholds in hypothyroid group were significantly higher than in healthy controls at 250 ($p<0.001$) and 500 Hz ($p=0.003$) (Table 2). Median audiometric threshold at 250 Hz was significantly higher in subclinical hypothyroidism group than in healthy controls ($p=0.001$). Higher audiometric thresholds at 250 ($p<0.001$), 500 ($p<0.001$), and 6000 Hz ($p=0.004$) were recorded in obvious hypothyroid group compared to control subjects. When we compared the thresholds between subclinical and obvious hypothyroidism groups, we found that patients with obvious hypothyroidism had higher thresholds at 1000 ($p=0.004$) and 4000 Hz ($p=0.001$) (Table 3). There were no differences between Hashimoto's thyroiditis group and partial thyroidectomy group with respect to audiometric findings (data are not shown).

In correlation analysis, TSH correlated positively with hearing thresholds at 250, 500, 2000, 4000, and 6000 Hz, while free T3 and free T4 correlated negatively with pure tone audiometric

findings at 250 and 500 Hz. No correlations were detected between hearing levels and anti-TPO and anti-Tg (Table 4). Sodium levels correlated positively with hearing threshold at 8000 Hz (rho=0.519, p=0.033) and calcium levels correlated negatively with hearing threshold at 6000 Hz (rho=-0.448, p<0.001). Systolic and diastolic blood pressures, glucose, lipid, potassium, and chlorine levels did not correlate with hearing thresholds.

Discussion

In our study, we revealed that hearing is impaired in patients with hypothyroidism. Additionally, a statistically significant relationship could be established between TSH and thyroid hormone levels and hearing thresholds. Both subclinical hypothyroidism and obvious hypothyroidism were found to affect hearing ability.

Table 1. Clinical and laboratory features of hypothyroid patients and healthy controls

Variables	Hypothyroid group (n=58)	Control group (n=34)	p-value
Age, years	35.29±10.45	35.73±8.37	0.834
Female/Male	54/4	29/5	0.224
Systolic BP, mmHg	120 (92-135)	120 (110-131)	0.751
Diastolic BP, mmHg	80 (60-85)	80 (70-90)	0.119
TSH, µIU/ml	11.70 (4.26-100)	1.44 (0.61-3.80)	**<0.001**
Free T4, ng/dl	0.63 (0.25-0.98)	0.84 (0.61-1.04)	**<0.001**
Free T3, pg/ml	2.86 (1.46-3.72)	3.25 (2.69-3.82)	**<0.001**
Anti-TPO, IU/ml	101.18 (0.35-1092)	1.10 (0.25-3.5)	**<0.001**
Anti-Tg, IU/ml	10.93 (0.9-4000)	10 (0.58-104.5)	**0.016**
Hemoglobin, g/dl	13.14±0.94	13.44±1.10	0.166
White blood cells, µ/l	6705.55±1639.42	6258.82±1755.70	0.227
Sedimentation, mm/h	12.15±5.90	12.18±10.25	0.989
Vitamin B12, pg/ml	217.44±73.37	219.03±76.25	0.927
Fasting glucose, mg/dl	82.6±7.3	82.4±6.2	0.840
Total calcium, mmol/l	9.20 (4.38-10.10)	9.30 (8.5-9.6)	0.803
Sodium, mmol/l	138 (135-144)	138 (135-144)	0.295
Potassium, mmol/l	4.19±0.29	4.17±0.23	0.673
Chlorine, mmol/l	104 (97-109)	104 (99-109)	0.977
Total cholesterol, mg/dl	179.62±35.91	180.14±39.35	0.950
Triglyceride, mg/dl	103.56±58.14	109.52±45.85	0.617
LDL-C, mg/dl	109.46±29.50	117.16±20.82	0.190
HDL-C, mg/dl	45.17±11.65	42.10±7.06	0.173

Data are means ± SD or median (minimum-maximum) or number of subjects. Bold p values indicate statistically significant (p<0.05). Anti-Tg: Thyroglobulin antibody, Anti-TPO: Thyroid peroxidase antibody, BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormone

Table 2. Comparison of pure tone thresholds between hypothyroid group and control group

	Hypothyroid group		Control group		
Frequencies (Hertz)	**Median (min-max)**	**Mean ± SD**	**Median (min-max)**	**Mean ± SD**	**p-value[a]**
250	10 (0-45)	13.91±8.70	5 (0-15)	7.73±3.77	**<0.001**
500	10 (0-40)	12.00±7.64	10 (-5-15)	8.28±4.81	**0.003**
1000	10 (0-50)	12.75±7.70	10 (0-20)	10.27±5.34	0.802
2000	5 (-5-50)	9.53±9.96	5 (0-40)	8.20±9.58	0.193
4000	10 (-10-55)	12.28±12.89	10 (-5-25)	9.21±7.92	0.348
6000	15 (-5-80)	20.04±15.51	15 (0-45)	14.84±9.59	0.059
8000	15 (0-50)	19.56±14.60	15 (5-35)	18.33±11.63	0.820

SD: Standard deviation, The data are given in dB hearing thresholds. Bold p values indicate statistically significant (p<0.05). [a]: Mann-Whitney U test

Patients with Hashimoto's thyroiditis did not differ from the patients with other etiological diagnosis of hypothyroidism in terms of hearing.

Previous clinical and experimental studies evaluating auditory functions in hypothyroidism using audiometry or electrophysiological methods, such as brainstem auditory evoked potentials and otoacoustic emissions have showed inhomogeneous results. A study by Ben-Towim et al. (3) conducted in rats with experimentally induced hypothyroidism detected changes in the amplitude and the latency of auditory potentials. Moreover, that study also showed that the changes in auditory potentials were directly associated with serum levels of free T4. The results of Di Lorenzo et al. (7) study showed changes in auditory brainstem responses in 25% of hypothyroid patients and also showed a relationship between the abnormalities in auditory potentials and the degree of hypothyroidism. Similar to that, Himmelfarb et al. (8) noted that hearing impairment in hypothyroid patients was significantly related to low free T4. Another study detected hearing impairment in 71.11% of patients with hypothyroidism (9). In a study by Thornton and Jarvis, (10) it has been reported that according to audiometry results, hypothyroid patients had a greater hearing loss than controls. In that study, 36% of hypothyroid patients had an elevated four frequency (500, 1000, 2000, and 4000 Hz) average threshold. On the other hand, the detected abnormalities in the brainstem auditory evoked potentials in hypothyroid patients were suggested to occur because of low body temperature seen in these patients rather than direct results of the hypothyroidism. In a study in which 70% of the patients had hypothyroidism secondary to Hashimoto's thyroiditis, high audiometric thresholds were recorded in 36.7% of hypothyroid patients and in only 11.67% of controls (11). The authors did not find any associations between audiometric thresholds and the serum levels of TSH and free T4

Table 3. Comparison of pure tone thresholds among subclinical hypothyroid group, obvious hypothyroid group, and control subjects

	Subclinical hypothyroid group (n=28)		Obvious hypothyroid group (n=30)		Control group (n=34)		p-value			
Frequencies (Hertz)	**Median (min-max)**	**Mean ± SD**	**Median (min-max)**	**Mean ± SD**	**Median (min-max)**	**Mean ± SD**	**Among the three groups***	**Subclinical hypothyroid group and control group†**	**Obvious hypothyroid group and control group†**	**Subclinical and obvious hypothyroid groups†**
250	10 (0-35)	11.94±7.42	15 (0-45)	15.96±9.50	5 (0-15)	7.73±3.77	**<0.001**	**0.001**	**<0.001**	0.020
500	10 (0-25)	10.00±5.31	10 (5-40)	14.05±9.04	10 (-5-15)	8.28±4.81	**0.001**	0.150	**<0.001**	0.024
1000	7.5 (0-20)	8.05±5.86	10 (0-50)	13.86±10.90	10 (0-20)	10.27±5.34	**0.010**	0.063	0.147	**0.004**
2000	5 (-5-25)	6.85±6.60	10 (0-50)	12.26±11.95	5 (0-40)	8.20±9.58	**0.027**	0.949	0.022	0.016
4000	5 (-10-55)	8.79±10.63	10 (-5-55)	15.84±14.06	10 (-5-25)	9.21±7.92	**0.003**	0.361	0.011	**0.001**
6000	15 (0-60)	16.11±11.27	20 (-5-80)	14.84±9.59	15 (0-45)	14.84±9.59	**0.007**	0.725	**0.004**	0.011
8000	15 (5-50)	20.00±13.58	10 (0-45)	24.13±18.16	15 (5-35)	18.33±11.63	0.852	-	-	-

The data are given in dB hearing thresholds. *: Kruskal-Wallis test, bold p values indicate statistically significant (p<0.05), †: Mann-Whitney U test with Bonferroni correction, bold p values indicate statistically significant (p<0.0083)

Table 4. Correlation of hearing thresholds (dB) with thyroid function tests and thyroid autoantibody levels

		250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	6000 Hz	8000 Hz
TSH	**rho**	0.398	0.301	0.104	0.207	0.195	0.214	-0.028
	p	**<0.001****	**<0.001****	0.183	**0.007****	**0.011***	**0.006****	0.864
Free T4	**rho**	-0.250	-0.179	-0.045	-0.040	-0.054	-0.132	0.119
	p	**0.001****	**0.021***	0.561	0.606	0.486	0.090	0.465
Free T3	**rho**	-0.256	-0.264	-0.129	-0.345	-0.199	-0.174	-0.078
	p	**0.004****	**0.003****	0.152	**<0.001****	**0.026***	0.054	0.677
Anti-TPO	**rho**	0.159	0.032	-0.070	-0.014	-0.072	-0.069	-0.023
	p	0.052	0.685	0.370	0.855	0.359	0.377	0.886
Anti-Tg	**rho**	0.072	-0.009	0.042	0.021	-0.057	-0.081	-0.022
	p	0.435	0.923	0.648	0.822	0.533	0.378	0.901

Bold p values indicate statistically significant. **: Correlation is significant p<0.01, *: Correlation is significant p<0.05, Anti-Tg: Thyroglobulin antibody, Anti-TPO: Thyroid peroxidase antibody, Hz: Hertz, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormone

(11). In the present study, we found that audiometric thresholds were higher at 250 and 500 Hz in patients with hypothyroidism compared to that in healthy subjects. Moreover, these hearing thresholds correlated positively with TSH, and negatively with thyroid hormones. Our findings suggest that there is a causal relationship between hypothyroidism and hearing impairment. In subclinical hypothyroidism, studies have shown conflicting results: hearing was either impaired (11,12) or remained unchanged (7,13) with subclinical hypothyroidism. In our study, hearing threshold at 250 Hz was higher in patients with subclinical hypothyroidism than in control subjects. In obvious hypothyroidism, hearing thresholds were significantly higher than in the healthy controls at 250, 500, and 6000 Hz. When we compared subclinical and obvious hypothyroid patients, obvious hypothyroid group had higher hearing thresholds at 1000 and 4000 Hz. Our findings suggest that both subclinical hypothyroidism and obvious hypothyroidism cause hearing impairment, but it seems that hearing is affected more in patients with obvious hypothyroidism, especially at higher frequencies.

The pathophysiological mechanism of hearing impairment in acquired hypothyroidism is not well understood. Hypothyroidism reduces the cell energy production, which causes a deterioration of oxygenation and metabolism in the inner ear structures, such as organ of Corti and stria vascularis. Additionally, thyroid hormones control production of enzymes and myelin in the central nervous system. Moreover, T4 can act as a neurotransmitter. Thus, hearing impairment in hypothyroidism has been suggested to originate in the cochlea, in the central auditory pathways, and/or in the retrocochlear region (7,11).

Higher prevalence of hypertension among patients with hypothyroidism may an important predisposing factor for hearing loss since it affects stria vascularis in cochlea which is very sensitive to pressure variations (14). In our study, no one had hypertension, and neither systolic nor diastolic blood pressures correlated with audiometric findings. Other important risk factors for hearing loss in hypothyroidism are changes in the biochemical tests. Dysglycemia which has been reported to affect the inner ear may cause hearing impairment in hypothyroidism (15,16). In our study, all participants had normal glucose levels, and there were no differences with respect to glucose levels between hypothyroid group and control subjects. Since higher audiometric thresholds have been reported in patients with lipid disorders, dyslipidemia due to hypothyroidism may also be one of the causes of hearing loss (17). By analyzing the results from this study, we found that hypothyroid patients and healthy controls had similar lipid levels, and lipid levels did not correlate with hearing thresholds. It is known that hypothyroidism decreases the intestinal absorption of some electrolytes, such as calcium which affects the synaptic transmission and hearing (18). In the present study, regarding serum calcium, all subjects were normocalcemic and no correlations of calcium levels with 250 and 500 Hz hearing frequencies were found. Based on all these findings, we suggest that blood pressure and biochemical parameters may not be directly responsible for the changed audiologic tests in patients with hypothyroidism.

In conclusion, our results suggest that hearing ability decreases in patients with acquired hypothyroidism regardless of having subclinical or obvious hypothyroidism. It seems that hearing impairment directly results from TSH and thyroid hormone alterations. However, further studies are needed to clarify the mechanism of hearing loss in patients with hypothyroidism.

Authorship Contributions

Ethics Committee Approval: The study were approved by Ankara Numune Research and Training Hospital of Local Ethics Committee, Informed Consent: Consent form was filled out by all participants, Concept: Ayşe Arduç, Design: Ayşe Arduç, Serhat Işık, Ayse İriz, Data Collection or Processing: Ayşe Arduç, Bercem Ayçiçek Doğan, Mazhar Müslim Tuna, Celil Göçer, Analysis or Interpretation: Ayşe Arduç, Dilek Berker, Serdar Güler, Literature Search: Serpil Alluşoğlu, Ayse İriz, Writing: Ayşe Arduç, Serpil Alluşoğlu, Peer-review: Externally peer-reviewed, Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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