Published online: 2020-01-28

An Investigation of Hearing (250–20,000 Hz) in Children with Endocrine Diseases and Evaluation of Tinnitus and Vertigo Symptoms

Murat Kocyigit[1] Selin Ustun Bezgin[1] Taliye Cakabay[1] Safiye Giran Ortekin[1] Melek Yıldız[2] Guven Ozkaya[3] Banu Aydın[2]

[1] Department of Otolaryngolgy, Istanbul Kanuni Sultan Suleyman Egitim ve Arastirma Hastanesi, Istanbul, Turkey
[2] Department of Pediatric Endocrinology, Istanbul Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey
[3] Department of Biostatistics, Uludag Universitesi Tip Fakultesi, Bursa, Turkey

Address for correspondence Murat Kocyigit, MD, Department of Otolaryngolgy, Istanbul Kanuni Sultan Suleyman Egitim ve Arastirma Hastanesi, Istanbul 34303, Turkey (e-mail: muratdr63@yahoo.com).

Int Arch Otorhinolaryngol 2020;24:e198–e205.

Abstract

Introduction Despite much advancement in medicine, endocrine and metabolic diseases remain an important cause of morbidity and even mortality in children.

Objective The present study was planned to investigate the evaluation of hearing that also includes high frequencies, and the presence and degree of vertigo and tinnitus symptoms in pediatric patients diagnosed with endocrine diseases such as type 1 diabetes mellitus (DM), growth hormone deficiency (GHD), obesity, idiopathic short stature, and precocious puberty

Methods The present study included a patient group of 207 children patients diagnosed with endocrine disease (95 males, 112 females; mean age 9.71 years old [range 6–16 years old]) and a control group including 55 healthy children who do not have any kind of chronic disease (26 males, 29 females; mean age 9.33 years old [range 6–16 years old]). The subjects underwent a hearing test with frequencies between 250 and 20,000 Hz. The vestibular and tinnitus symptoms were evaluated with the Pediatric Vestibular Symptom Questionnaire.

Results Out of 207 patients in the patient group, 5 (2.4%) had hearing loss in pure tones, 10 (4.8%) had it in high frequencies, 40 (19.3%) had tinnitus symptoms, and 18 (8.7%) had vertigo symptoms. A total of 4 out of 207 patients in the study group (1.9%), 2 out of 59 with type 1 DM patients (3.4%), 1 out of 46 with GHD (2.2%), and 1 out of 43 obesity patients (2.3%) had hearing loss, vertigo, and tinnitus symptoms.

Conclusions Our results suggest that some childhood endocrine diseases can cause some changes in the inner ear, although the exact cause is unknown. Perhaps, a detailed hearing and balance examination should be a routine in a child diagnosed with an endocrine disease. We think it is necessary to work on more comprehensive patient groups and tests in the future.

Keywords
- Endocrinology
- pediatric
- hearing level
- tinnitus
- vertigo

received
March 14, 2019
accepted
August 18, 2019

DOI https://doi.org/10.1055/s-0039-1698775.
ISSN 1809-9777.

Introduction and Objective

Despite much advancement in medicine, endocrine and metabolic diseases remain an important cause of morbidity and even mortality in children. Comorbidities accompanying these diseases may be as detrimental as the diseases themselves. Comorbidities associated with inner ear functions are also seen. Diabetes mellitus (DM) is characterized by hyperglycemia. Diabetes mellitus is a genetically defined metabolic disease, and it may cause vascular and neuropathic complications due to its metabolic effects.[1] More than 90% of all children with DM have Type I, which frequently presents in adolescence.[2] There are many studies on damage caused by Type 1 DM (T1DM) in the cochlear and retrocochlear pathways of the auditory pathway.[3,4] Growth hormone deficiency (GHD) is a rare disease which is seen in 1 in between 3,840 and 10,000 live births.[5,6] Growth hormone deficiency is mostly diagnosed and treated during childhood; therefore, it is not easy to clearly detect the effect of GHD on hearing. There are studies showing that growth hormone (GH) affects the development and functions of the auditory system in humans[7–9] and in several animal species.[10–12] Childhood obesity (OB) is a serious public health issue, and 17% of the children in the US have been reported to be obese (body mass index BMI $>$ 30). One third of the adolescents with OB have metabolic syndrome and comorbidities.[13,14] In adults, OB and accompanying comorbidities have been determined to be a risk factor for hearing loss.[15–17] Short stature (SS) in children is one of the common reasons for seeking help from pediatric endocrinologists. As no etiological cause can be found in most of these cases, they are termed idiopathic short stature (ISS). Precocious puberty (PP) is seen 8- to 10-fold more frequently in girls than in boys, and is characterized by breast budding in girls before the age of 8 years old and testicular enlargement in boys before the age of 9 years old. Patients with ISS and precocious PP are frequently seen in pediatric endocrinology outpatient clinics and consist a heterogeneous group.[18–20] The present study was planned to investigate the evaluation of hearing that also includes high frequencies, and the presence and degree of vertigo and tinnitus symptoms in pediatric patients diagnosed with endocrine diseases such as T1DM, GHD, OB, ISS, and PP.

Materials and Methods

The present study included 207 pediatric patients (95 males, 112 females; mean age 9.70 years old [range 6–16 years old] who were being followed-up in our pediatric endocrinology clinic for T1DM (with diagnosis duration $>$ 5 years and with controlled disease), GHD, OB, ISS, PP, and a healthy control group of 55 children without any chronic disease (26 males, 29 females; mean age 9.38 years old [range 6–16 years old]). The study was prepared in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board. The study was approved by Clinical Research Ethics Committee (approval number: KAEK/2018/07/07). Patients who did not meet the study inclusion criteria were excluded to avoid bias.

Inclusion Criteria for the Study Group:

- Being between 6 and 16 years old
- Having one of the following endocrine diseases: T1DM, GHD, OB, ISS or PP

Exclusion Criteria for the Study Group:

- Mental retardation
- Having a syndrome with a vestibulocochlear system anomaly
- Current upper respiratory tract infection
- Active inflammation or effusion in the middle ear
- Wax in ears
- History of ear surgery or adenotonsillectomy
- History of another known chronic disease
- Absence of thyroid disease

Informed written consent was obtained from the parents of the studied children after explanation of the purpose of the research. All of the children underwent a complete otolaryngologic examination, and the ears were checked using an otoscope. Tympanometry was performed by an audiologist using a MAICO m40 Tympanometer device (Maico Diagnostics GmbH, Berlin, Germany). Hearing tests for the subjects in the study and control groups were performed in anechoic rooms following the Industrial Acoustics Company (IAC) standard using a MAICO m42 audiometry device (Maico Diagnostics GmbH, Berlin, Germany) with air conduction hearing test being performed between the frequencies of 250 and 20,000 Hz, bone conduction hearing test between the frequencies of 500 and 4,000 Hz, acoustic reflex recording, and pure tone average (PTA) consisting of 500, 1,000, 2,000, and 4,000 Hz frequencies, and high frequency average (HFA) consisting of 8,000, 10,000, 12,000, 16,000, and 20,000 Hz frequencies being recorded. Subjects with conductive hearing loss detected in the audiometry tests and ears with a tympanogram result of Type B or Type C were excluded from the study. The tests were performed in both ears, and since the difference between the 2 ears was $<$ 10 dB in almost all of the frequencies, the results were evaluated as a single ear. The normal hearing level was considered as between 0 and 20 dB, and a hearing level $>$ 20 dB was considered as hearing loss. As there was no "Turkish, vestibular symptom questionnaire" with international validity in the pediatric patient group, the "Turkish-translated version" of the Pediatric Vestibular Symptom Questionnaire (PVSQ) form,[21] which is a well-accepted form in the literature, was used. The answers in this questionnaire form consisting of 10 questions in which "mostly" = 3, "sometimes" = 2, "hardly ever" = 1," "never" = 0, and "I don't know. The patients filling the form chose the answer applying to them. The scores of the answers given to the 10 questions were summed up, and a total score between 0 and 15 was considered to be normal, and a total score between 15 and30 was considered to be vertigo symptom (PVSQS+). Other than this form, for tinnitus evaluation, the patients were requested to answer the question "Do you have complaints of humming, ringing and noise in your ears?" by choosing one of the following options: of "mostly" = 3, "sometimes" = 2, "hardly ever" = 1," "never"

= 0, and "I don't know", corresponding to what applied to them. Patients who answered 2 or 3 to the tinnitus question were considered to have tinnitus symptom (TIN +). Patients with missing answers or who answered "I don't know" were excluded from the study.

Statistical Analysis

All of the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used as normality test. For non-normally distributed data, continuous variables were compared using the Mann-Whitney U test. Categorical variables were compared using the Pearson chi-squared test and the Fisher exact test. A p-value < 0.05 was considered to be significant.

Results

When 207 patients in the study group (including 5 subgroups) and 55 subjects in the healthy control group were compared for age and gender, there was no statistically significant difference. ►**Table 1** shows the age and gender distribution, and PTA and HFA values of the study and the control groups. Out of 207 patients in the study group, 59 (28.5%) had T1DM, 46 (22.2%) had GHD, 43 (20.8%) had OB, 37 (17.9%) had ISS, and 22 (10.6%) had PP. ►**Table 2** shows the

Table 1 Age and sex distribution of study and control groups, pure tone average, high frequency average values

	Control Group	Type1 DM	GH deficiency	Obesity	Idiopathic short stature	Precocious Puberty	Total study group
Number rate (%)	55 (100%)	59 (28.5%)	46 (22.2%)	43 (20.8%)	37 (17.9%)	22 (10.6%)	207 (100%)
Boy/girl (*n*)	26/29	28/31	22/24	22/21	18/19	5/17	95/112
Boy/girl rate (%)	47.3/52.7	46.9/53.1	47.8/52.2	51.2/48.8	48.6/51.4	22.7/77.3	45.9/54.1
Age average (years old)	9.33	9.03	9.35	9.63	9.57	8.36	9.71
Pure tone average	3.11	5.33	4.04	5.05	3.58	3.69	4.51
High frequency average	4.35	7.29	5.57	6.72	4.03	4.55	5.91

Table 2 In pure tones and high frequencies, mean, minimum and maximum hearing values

		Pure Tones 250–500–1000 –2,000–4,000 Hz	High Frequencies 8,000–10,000–12,000-16,000–20,000 Hz
Control Group	*n*	55	55
	Mean ± SD	3.11 ± 4.58	4.35 ± 6.48
	Minimum–Maximum	0.00–31.25	0.00–49
Type 1 diabetes mellitus	*n*	59	59
	Mean ± SD	5.33 ± 6.01	7.29 ± 9.35
	Minimum–Maximum	0.00–31.25	0.00–51.00
Growth hormone deficiency	*n*	46	46
	Mean ± SD	4.04 ± 5.13	5.57 ± 7.55
	Minimum–Maximum	0.00–28.75	0.00–38
Obesity	*n*	43	43
	Mean ± SD	5.05 ± 6.06	6.72 ± 10.26
	Minimum–Maximum	0.00–27.50	0.00–59
Idiopathic short stature	*n*	37	37
	Mean ± SD	3.58 ± 3.69	4.03 ± 3.01
	Minimum–Maximum	0.00–15.00	0.00–13.00
Precocious puberty	*n*	22	22
	Mean ± SD	4.21 ± 5.13	5.58 ± 7.64
	Minimum–Maximum	0.00–31.25	0.00–59.00

Table 3 Number, Rate, and p-value of PTA, HFA, PTA&HFA values of more than 20 dB in study and control groups

	Control Group $n=55$	Type1 DM $n=59$	GH Deficiency $n=46$	Obesity $n=43$	Id. Short Stature $n=37$	Prec. Puberty $n=22$	Total Study Group $n=207$
PTA > 20dB	1/1.8%	2/3.4% $p=1.000$	1/2.7% $p=1.000$	2/4.7% $p=0.580$	0/0% $p=1.000$	0/0% $p=1.000$	5/2.4% $p=1.000$
HFA > 20dB	1/1.8%	4/6.8% $p=0.365$	3/6.5% $p=0.328$	3/7.0% $p=0.316$	0/0% $p=1.000$	0/0% $p=1.000$	10/4.8% $p=0.467$
PTA&HFA > 20dB	1/1.8%	2/3.4% $p=1.000$	1/2.7% $p=1.000$	2/4.7% $p=0.580$	0/0% $p=1.000$	0/0% $p=1.000$	5/2.4% $p=1.000$

Abbreviations: HFA, high frequency average; PTA, pure tone average.
*A p-value < 0.05 was considered as significant.

pure tones and high frequencies, mean, minimum and maximum hearing values.

Patients with a PTA, HFA or both PTA and HFA values (PTA&HFA) value > 20 dB were considered to have hearing loss. Out of 207 patients in the whole study group, 5 (2.4%) had a PTA value > 20 dB, 10 (4.8%) had HFA value > 20 dB, and 5 (2.4%) had a PTA&HFA value > 20 dB. No statistically significant difference was detected between the whole study and the control groups for PTA, HFA and PTA&HFA values being > 20 ($p = 1.000$; 0.467; and 1.000, respectively). When T1DM, GHD, OB, ISS and PP patients were individually compared with the control group for PTA, HFA and PTA&HFA values being > 20 dB, the difference was not statistically significant ($p > 0.05$). ►**Table 3** shows the number, the percentage and the p-value of the subjects with a PTA, HFA, PTA&HFA value > 20 dB in the study and control groups.

While hearing loss (> 20 dB) was detected in different numbers in the whole study group and the subgroups when evaluated individually for each studied frequency (250–20,000 Hz), none of these were statistically significantly different compared with the control group ($p > 0.05$). ►**Table 4** shows the number of subjects, percentage, and the p-value with a hearing level of > 20 dB at each studied frequency.

Out of 207 patients in the whole study group, 40 (19.3%) had tinnitus symptoms and 18 (8.7%) had vertigo symptoms. When the patients in the 5 subgroups which constitute the study group were assessed individually, tinnitus and vertigo symptoms rates were varying; however, compared with the control group, there was no statistically significant difference both for the whole study group and for the subgroups, except for ISS patients (9/37 ISS patients [24.3%] had tinnitus symptoms, $p = 0.046$). ►**Table 5** shows the Tinnitus symptoms and PVSQS values of the study and control groups.

A total of 6 out of 207 patients in the study group (2.9%), 3 out of 59 T1DM patients (5.1%), 2 out of 46 GHD patients (4.3%), and 1 out of 43 OB patients (2.3%) had a PTA&HFA value of >20 dB and vertigo symptoms (patients with both PTA and HFA > 20 dB together with PVSQS +), and none of the ISS and PP patients had a PTA&HFA value of > 20 dB and vertigo symptoms. A total of 4 out of 207 patients in the study group (1.9%), 2 out of 59 T1DM patients (3.4%), 1 out of 46 GHD patients (2.2%), 1 out of 43 OB patients (2.3%) had a PTA&HFA value >20 dB and vertigo and tinnitus symptoms (patients with both PTA and HFA > 20 dB together with PVSQS+ and TIN +), and none of the ISS and PP patients had a PTA&HFA value of > 20 dB and vertigo and tinnitus symptoms (►**Table 6**).

Discussion

There are some studies in the literature that are not very comprehensive showing that hearing loss and vestibular system involvement may be seen in endocrine and metabolic diseases.[22–24] In the present study, we planned to investigate the evaluation of hearing that also includes high frequencies, and the presence and degree of vertigo and tinnitus symptoms in pediatric patients diagnosed with endocrine diseases such as T1DM, GHD, OB, ISS, and PP.

Diabetes mellitus is a genetically defined metabolic disease, and it may cause vascular and neuropathic complications due to its metabolic effects.[1] Diabetes mellitus is characterized by hyperglycemia. More than 90% of all DM patients have Type I, and the disease frequently present in adolescence.[2] Type 1 DM almost always involves a complete insulin deficiency. There are many studies on the damage caused by DM in the cochlear and retrocochlear pathways of the auditory pathway.[3,4,25–27] As with many metabolic diseases, neuropathy and angiopathy are also common outcomes of DM.[2] Glucose is a substantial energy source for nerve tissue. Many investigators have performed studies on hearing functions in DM, and claimed that auditory neuropathy in DM has a similar pathogenesis with peripheral diabetic neuropathy. While DM-induced nervous system pathologies are mainly seen in the peripheral nervous system, there are also many studies showing changes in the central nervous system (CNS). Histopathologic studies in DM patients have reported pathologies including atrophy of the spiral ganglion due to microangiopathy in the auditory pathways; hemorrhage in the endolymph, perilymph and modiolus; hair cell damage in the organ of Corti; neuropathy in the auditory nerve; demyelination and damage in the central auditory pathways.[3,28,29] This shows that DM may cause hearing loss at varying degrees by affecting almost all components of hearing.[3] Moreover, in their study, Reske-Nielsen reported obstruction in the vasa vasorum and fibrosis in the perineurium.[30] A different explanation for central

Table 4 Number, Rate, and p-value of persons with hearing level > 20 dB at viewed frequencies

	Control Group $n = 55$	Type1 diabetes mellitus $n = 59$	Growth hormone deficiency $n = 46$	Obesity $n = 43$	Idiopathic short stature $n = 37$	Precocious puberty $n = 22$	Total study group $n = 207$
250 Hz	0 (0%)	0 (0%) No p-value	0 (0%) No p-value	0 (0%) No p-value	0 (0%) No p-value	0 (0%) No p-value	0 (0%) No p-value
500 Hz	1 (1.8%)	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	0 (0%) $p = 0.210$
1,000 Hz	1 (1.8%)	2 (3.4%) $p = 1.000$	1 (2.2%) $p = 1.000$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	4 (1.9%) $p = 1.000$
2,000 Hz	1 (1.8%)	2 (3.4%) $p = 1.000$	1 (2.2%) $p = 1.000$	2 (4.7%) $p = 0.580$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	5(2.4%) $p = 1.000$
4,000 Hz	1 (1.8%)	2 (3.4%) $p = 1.000$	1 (2.2%) $p = 1.000$	2 (4.7%) $p = 0.580$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	5(2.4%) $p = 1.000$
8,000 Hz	1 (1.8%)	4 (6.8%) $p = 0.365$	3 (6.5%) $p = 0.328$	2 (4.7%) $p = 0.580$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	9 (4.3%) $p = 0.693$
10,000 Hz	1 (1.8%)	4 (6.8%) $p = 0.365$	3 (6.5%) $p = 0.328$	3 (7.0%) $p = 0.316$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	10 (4.8%) $p = 0.467$
12,000 Hz	1 (1.8%)	4 (6.8%) $p = 0.365$	3 (6.5%) $p = 0.328$	3 (7.0%) $p = 0.316$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	10 (4.8%) $p = 0.467$
16,000 Hz	1 (1.8%)	4 (6.8%) $p = 0.365$	3 (6.5%) $p = 0.328$	3 (7.0%) $p = 0.316$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	10 (4.8%) $p = 0.467$
20,000 Hz	1 (1.8%)	4 (6.8%) $p = 0.365$	3 (6.5%) $p = 0.328$	3 (7.0%) $p = 0.316$	0 (0%) $p = 1.000$	0 (0%) $p = 1.000$	10 (4.8%) $p = 0.467$

*A p-value < 0.05 was considered as significant.

Table 5 Demonstration of Tinnitus and Pediatric Vestibular Symptom Questionnaire Score Values, Rate, and p-value in the study and control groups

		Control Group $n = 55$	Type1 diabetes mellitus $n = 59$	Growth hormone deficiency $n = 46$	Obesity $n = 43$	Idiopathic short stature $n = 37$	Precocious puberty $n = 22$	Total study group $n = 207$
Tinnitus symptoms scores	**0 or 1**	50 (90.9%)	48 (81.4%)	39 (84.8%)	34 (79.1%)	28 (75.7%)	18 (81.8%)	167 (80.7%)
	2 or 3 (Tinnitus sympoms)	5 (9.1%)	11 (18.6%) $p = 0.142$	7 (15.2%) $p = 0.343$	9 (20.9%) $p = 0.096$	9 (24.3%) $\mathbf{p = 0.046}$	4 (18.2%) $p = 0.267$	40 (19.3%) $p = 0.074$
Pediatric vestibular symptom questionnaire score **symptoms**	**0–15**	53 (96.4%)	53 (89.8%)	43 (93.5%)	37 (86.0%)	36 (97.3%)	20 (90.9%)	189 (91.3%)
	16–30 (Vertigo symptoms)	2 (3.6%)	6 (10.2%) $p = 0.274$	3 (6.5%) $p = 0.657$	6 (14.0%) $p = 0.133$	1 (2.7%) $p = 1.000$	2 (9.1%) $p = 0.574$	18 (8.7%) $p = 0.265$

*A p-value <0.05 was considered as significant.

neural conduction is the possibility of the electroconduction of myelin sheath being damaged as a response to the various metabolic changes caused by DM.[31] While many investigators have reported that DM patients have worse hearing,[3,32,33] some claimed the opposite and stated there was no such relationship.[27,34] Di Nardo et al reported between ~ 5 and 30 dB loss at all frequencies, mainly at between 4 and 8 kHz.[3] Lasisi et al detected vestibulocochlear complications in 189 out of 240 patients (79%) diagnosed with DM between the ages of 13 and 90 years old.[33] In our study, the PTA value of 59 T1DM patients was 5.33, and the HFA value was 7.29; 2 patients (3.4%) had hearing loss in pure tones, 4 patients (6.8%) had hearing loss in high frequencies, 2 patients (3.4%) had hearing loss both in pure tones and high frequencies, 11 patients (18.6%) had tinnitus symptoms, 6 patients (10.2%) had vertigo symptoms, 3 patients (5.1%) had hearing loss together with vertigo symptoms, 2 patients (3.4%) had hearing loss together with vertigo and tinnitus symptoms.

Table 6 Demonstration of hearing loss and/or vertigo and/or tinnitus symptoms in the control and study groups as patient number, percentage, and p-value

	Control Group $n = 55$	Type1 diabetes mellitus $n = 59$	Growth hormone deficiency $n = 46$	Obesity $n = 43$	Idiopathic short stature $n = 37$	Precocious puberty $n = 22$	Total study group $n = 207$
PTA&HFA > 20dB +Vertigo symptoms	0 (0%)	3 (5.1%) $p = 0.244$	2 (4.3%) $p = 0.205$	1 (2.3%) $p = 0.439$	0 (0%) No p-value	0 (0%) No p-value	6 (2.9%) $p = 0.349$
PTA&HFA > 20dB +Vertigo +Tinnitus symptoms	0 (0%)	2 (3.4%) $p = 0.496$	1 (2.2%) $p = 0.455$	1 (2.3%) $p = 0.439$	0 (0%) No p-value	0 (0%) No p -alue	4 (1.9%) $p = 0.582$

Abbreviations: HFA, high frequency average; PTA, pure tone average; PTA&HFA, pure tone average and high frequency average
*A p-value < 0.05 was considered as significant.

When hearing loss was assessed by frequencies, none of the patients had loss at 250 and 500 Hz, 2 patients (3.4%) had hearing loss at 1,000, 2,000, and 4,000 Hz, and 4 (6.8%) at 8,000, 10,000, 12,000, 16,000, and 20,000 Hz. While no statistically significant difference was detected when all these results were compared with the control group, they indicated that T1DM causes certain function loss in the inner ear.

Growth hormone deficiency is a rare disease which is seen in 1 in between 3,840 and 10,000 live births.[5,6] There are studies showing that GH affects the development and functions of the auditory system in humans[7–9] and in several animal species.[10–12] Growth hormone deficiency is mostly diagnosed and treated during childhood; therefore, it is not easy to clearly detect the effect of GHD on hearing. Prado-Barreto et al compared 26 adult GHD patients (age: 47.6 ± 15.1 years old; 13 women) with healthy subjects for hearing, and reported that their hearing level is higher than the control group at 250 Hz ($p = 0.005$), 500 Hz ($p = 0.006$), 3 KHz ($p = 0.008$), 4 KHz ($p = 0.038$), 6 KHz ($p = 0.008$), and 8 KHz ($p = 0.048$), and misophonia and dizziness complaints are seen at higher rates than in the control group ($p = 0.011$), as well as mild hearing loss at high tones ($p = 0.029$). They also stated that it is unclear whether the dizziness detected in the patients is caused by vestibular insufficiency or cardiac problems.[35] Muus et al reported that out of 209 pediatric patients diagnosed with GHD, 173 (83%) had hearing loss, with 79% being bilateral and 21% being unilateral (hearing loss is present in a total of 309 ears). Additionally, in that study, compared with the patients with all types of loss, the PTA value was detected to be higher in patients with mixed type hearing loss.[36] In our study, the PTA value of 46 GHD patients was 4.04, and their HFA value was 5.57; 1 patient (2.2%) had hearing loss in pure tones ($p = 1.000$), 3 patients (6.5%) had hearing loss in high frequencies ($p = 0.328$), 1 patient (2.2%) had hearing loss both in pure tones and high frequencies ($p = 1.000$), 7 patients (15.2%) had tinnitus symptoms ($p = 0.343$), 3 patients (6.5%) had vertigo symptoms ($p = 0.657$), 2 patients (4.3%) had hearing loss and vertigo symptoms ($p = 0.205$), 1 patient (2.2%) had hearing loss with vertigo and tinnitus symptoms ($p = 0.455$). When hearing loss was assessed by frequencies, none of the patients had loss at 250 and 500 Hz, 1 patient (2.2%) had hearing loss at 1,000, 2,000, and 4,000 Hz, and 3 (6.5%) at 8,000, 10,000, 12,000, 16,000, and 20,000 Hz. As with T1DM patients in our study, the results obtained in GHD patients were not statistically significant; however, they indicate a negative effect on inner ear functions.

Childhood OB is a serious public health issue, and 17% of the children in the US have been reported to be obese (BMI > 30)[13]. One third of the adolescents with OB have metabolic syndrome and comorbidities.[14] In adults, OB and accompanying comorbidities have been determined to be a risk factor for hearing loss.[15–17] Obesity may cause hearing loss, directly or indirectly. As adipose tissue secretes hormones and cytokines, it may directly contribute to end-organ damage.[37] Adiponectin, which is believed to have anti-inflammatory and anti-atherogenic properties, is one of the most studied adipocytokines.[38] Low plasma concentrations of adiponectin in children have been demonstrated to be associated with OB.[39] Low adiponectin levels in adults have been demonstrated to be effective on high-frequency hearing loss. In addition to its direct effect, OB may also cause hearing loss indirectly with accompanying comorbidities such as type 2 DM, cardiovascular diseases and dyslipidemia, which have been shown to have negative effects on hearing.[40,41] The results of the previous studies investigating the relationship between OB and hearing loss are controversial. While some studies have reported that there is no direct relationship between OB and hearing loss,[42,43] others have reported the opposite.[37,39] Additionally, there is still no clear information as to the age and sex group in which OB causes more hearing loss, and the frequencies at which hearing loss is seen.[44,45] In our study, the PTA value of 43 OB patients was 5.05, and the HFA value was 6.72; 2 patients (4.7%) had hearing loss in pure tones, 3 patients (7.0%) had hearing loss in high frequencies, 2 patients (4.7%) had hearing loss both in pure tones and high frequencies, 9 patients (20.9%) had tinnitus, 6 patients (10.2%) had vertigo symptoms ($p = 0.133$), 1 patient (2.3%) had hearing loss with vertigo and tinnitus symptoms ($p = 0.439$). When hearing loss was assessed by frequencies, none of the patients had loss at 250, 500, or 1,000 Hz, 2 patients (4.7%) had hearing loss at 1,000, 2,000, and 4,000 Hz ($p = 0.580$) and 3 (7.0%) at 8,000, 10,000, 12,000, 16,000, and

20,000 Hz ($p = 0.316$). While the results obtained in patients with OB were not statistically significant, they still indicated a negative effect of OB on in the inner ear.

Short Stature (SS) in children is one of the common reasons of seeking help from pediatric endocrinologists. As no etiological cause can be found in most of these cases, they are termed ISS. Idiopathic short stature is having a short stature in individuals with normal birthweight, normal body ratios, normal GH secretion and no specific cause for short stature. Children with familial short stature, and constitutional delay of growth and puberty are also included into the ISS category.[18,19] There is no study showing the effect of ISS on hearing or balance. In our study, 37 ISS patients had a PTA value of 3.58, a HFA value of 4.03, and none of them had hearing loss at pure tones or high frequencies. A total of 9 ISS patients (24.3%) had tinnitus symptoms ($p = 0.046$), and 1 ISS patient (2.7%) had vertigo symptoms ($p = 1.000$). Precocious puberty is seen 8- to 10-fold more frequently in girls than in boys, and it is characterized by breast budding in girls before the age of 8 years old and testicular enlargement in boys before the age of 9 years old.[20] While there is no study showing that PP patients with no additional comorbidity have hearing loss or inner ear involvement, there are case reports showing hearing loss in cases with PP together with certain comorbidities or syndromes.[46,47] In our study, 22 PP patients had a PTA value of 3.69, a HFA value of 4.55, and none of them had hearing loss at pure tones or high frequencies. A total of 9 PP patients (18.2%) had tinnitus symptoms ($p = 0.267$), and 2 PP patients (9.1%) had vertigo symptoms ($p = 0.574$). While hearing loss was not seen in patients with ISS and PP, high rates of tinnitus and vertigo symptoms indicated a possible effect of these diseases on inner ear or interrelated comorbidities.

Out of 207 patients in the whole study group, 5 (2.4%) had a PTA value $>$ 20 dB, 10 (4.8%) had a HFA value $>$ 20 dB, and 5 (2.4%) had a PTA&HFA value $>$ 20 dB. While hearing loss ($>$ 20 dB) was detected at different numbers in the whole study group when evaluated individually for each studied frequency (250–20,000Hz), none of these were statistically significantly different compared with the control group ($p > 0.05$). Out of 207 patients in the whole study group, 40 (19.3%) had tinnitus symptoms, 18 (8.7%) had vertigo symptoms, 6 (2.9%) had hearing loss and vertigo symptoms, 4 (1.9%) had hearing loss with vertigo and tinnitus symptoms. While these results were not statistically significant, it suggested an inner ear involvement in patients diagnosed with endocrine diseases.

Our aim was to evaluate hearing in pediatric patients diagnosed with endocrine diseases such as T1DM, GHD, OB, ISS, and PP. Hearing is one of the functions of the inner ear, and tinnitus symptoms may also occur when hearing is affected. Vertigo symptoms can be seen in pathologies affecting the inner ear. We evaluated tinnitus and vertigo only with a symptom questionnaire and determined the presence and degree of symptoms. We know that we did not perform advanced objective tests such as videonystagmography, head impulse test, and vestibular evoked myogenic potential for vertigo. If we had performed these objective tests, the study might have been more specific, but we believe that it would be valuable in pediatric patients with different endocrinological diagnoses, due to lack of such a study. However, our study may be valuable as it is the first study to evaluate the hearing functions of pediatric patients with different endocrine diseases, as well as both vertigo and tinnitus symptoms. We believe that our work may be the beginning of future studies in this field and the study contributes to the literature.

Conclusion

Our results suggest that some childhood endocrine diseases can cause some changes in the inner ear, although the exact cause is unknown. Perhaps, a detailed hearing and balance examination should be a routine in a child diagnosed with an endocrinologic disease. We think it is necessary to work on more comprehensive patient groups and tests in the future.

Compliance with Ethical Standards

Ethics Committee Approval

The study was approved by the Institutional Review Board.

Informed Consent

Informed written consent was obtained from the parents of the children studied after explanation of the purpose of the research.

Research Involving Human Participants and/or Animals

All of the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Financial Disclosure

The authors declared that this study received no financial support.

Conflicts of Interests

The authors have no conflicts of interests to declare.

References

1 Maia CAS, Campos CAH. Diabetes mellitus as etiological factor of hearing loss. Rev Bras Otorrinolaringol (Engl Ed) 2005;71(02): 208–214
2 Funk JL. Pathopliydi'dogyof diseases. Yavuz A (Çev), 4th Edition. Ankara: Palme Publishing; 2006:244–251
3 Di Nardo W, Ghirlanda G, Paludetti G, et al. Distortion-product otoacoustic emissions and selective sensorineural loss in IDDM. Diabetes Care 1998;21(08):1317–1321
4 Di Leo MAS, Di Nardo W, Cercone S, et al. Cochlear dysfunction in IDDM patients with subclinical peripheral neuropathy. Diabetes Care 1997;20(05):824–828
5 Lindsay R, Feldkamp M, Harris D, Robertson J, Rallison M. Utah Growth Study: growth standards and the prevalence of growth hormone deficiency. J Pediatr 1994;125(01):29–35
6 Dorigueto RS, Mezzalira R, Serra AP. Semiology of hearing and balance. In: Caldas Neto S, Mello Ju'nior JF, Martins RHG, Costa SS,

eds. Tratado de Otorrinolaringologia. Vol I. 2nd ed. São Paulo, Brazil: ed Roca; 2011:362–79
7 Bonapace G, Concolino D, Formicola S, Strisciuglio P. A novel mutation in a patient with insulin-like growth factor 1 (IGF1) deficiency. J Med Genet 2003;40(12):913–917
8 Walenkamp MJ, Karperien M, Pereira AM, et al. Homozygous and heterozygous expression of a novel insulin-like growth factor-I mutation. J Clin Endocrinol Metab 2005;90(05):2855–2864
9 Attias J, Zarchi O, Nageris BI, Laron Z. Cochlear hearing loss in patients with Laron syndrome. Eur Arch Otorhinolaryngol 2012; 269(02):461–466
10 Camarero G, Villar MA, Contreras J, et al. Cochlear abnormalities in insulin-like growth factor-1 mouse mutants. Hear Res 2002; 170(1-2):2–11
11 Camarero G, Avendano C, Fernandez-Moreno C, et al. Delayed inner ear maturation and neuronal loss in postnatal Igf-1-deficient mice. J Neurosci 2001;21(19):7630–7641
12 Armstrong CS, Wuarin L, Ishii DN. Uptake of circulating insulin-like growth factor-I into the cerebrospinal fluid of normal and diabetic rats and normalization of IGF-II mRNA content in diabetic rat brain. J Neurosci Res 2000;59(05):649–660
13 Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. JAMA 2012;307(05):483–490
14 de Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the Third National Health and Nutrition Examination Survey. Circulation 2004;110(16):2494–2497
15 Gates GA, Cobb JL, D'Agostino RB, Wolf PA. The relation of hearing in the elderly to the presence of cardiovascular disease and cardiovascular risk factors. Arch Otolaryngol Head Neck Surg 1993;119(02):156–161
16 Barrenäs ML, Jonsson B, Tuvemo T, Hellström PA, Lundgren M. High risk of sensorineural hearing loss in men born small for gestational age with and without obesity or height catch-up growth: a prospective longitudinal register study on birth size in 245,000 Swedish conscripts. J Clin Endocrinol Metab 2005;90 (08):4452–4456
17 Fransen E, Topsakal V, Hendrickx JJ, et al. Occupational noise, smoking, and a high body mass index are risk factors for age-related hearing impairment and moderate alcohol consumption is protective: a European population-based multicenter study. J Assoc Res Otolaryngol 2008;9(03):264–276, discussion 261–263
18 Rogol AD, Hayden GF. Etiologies and early diagnosis of short stature and growth failure in children and adolescents. J Pediatr 2014;164(5, Suppl)S1–14.e6
19 Allen DB, Cuttler L. Clinical practice. Short stature in childhood–challenges and choices. N Engl J Med 2013;368(13):1220–1228
20 Bierich JR. Sexual precocity. Clin Endocrinol Metab 1975;4(01): 107–142
21 Pavlou M, Whitney S, Alkathiry AA, et al. The Pediatric Vestibular Symptom Questionnaire: A Validation Study. J Pediatr 2016; 168:171–7.e1
22 Vartiainen E, Karjalainen S. Prevalence and etiology of unilateral sensorineural hearing impairment in a Finnish childhood population. Int J Pediatr Otorhinolaryngol 1998;43(03):253–259
23 Duck SW, Prazma J, Bennett PS, Pillsbury HC. Interaction between hypertension and diabetes mellitus in the pathogenesis of sensorineural hearing loss. Laryngoscope 1997;107(12 Pt 1):1596–1605
24 D'Silva LJ, Lin J, Staecker H, Whitney SL, Kluding PM. Impact of diabetic complications on balance and falls: Contribution of the vestibular system. Phys Ther 2016;96(03):400–409. DOI: 10.2522/ptj.20140604
25 Ugur AK, Kemaloglu YK, Ugur MB, et al. Otoacoustic emissions and effects of contralateral white noise stimulation on transient evoked otoacoustic emissions in diabetic children. Int J Pediatr Otorhinolaryngol 2009;73(04):555–559
26 Gibbin KP, Davis CG. A hearing survey in diabetes mellitus. Clin Otolaryngol Allied Sci 1981;6(05):345–350
27 Harner SG. Hearing in adult-onset diabetes mellitus. Otolaryngol Head Neck Surg 1981;89(02):322–327
28 Kovar M. The inner ear in diabetes mellitus. ORL J Otorhinolaryngol Relat Spec 1973;35(01):42–51
29 Triana RJ, Suits GW, Garrison S, et al. Inner ear damage secondary to diabetes mellitus. I. Changes in adolescent SHR/N-cp rats. Arch Otolaryngol Head Neck Surg 1991;117(06):635–640
30 Reske –Nielsen E. Lundback K, Rafaelsen O. Pathological changes in the central and peripheral nervous system of young long-term diabetics. Diabetic encephalopaty. Diabetologia 1965I:233–241
31 Namyslowski G, Morawski K, Kossowska I, Lisowska G, Koehler B, Jarosz-Chobot P. Contralateral suppression of TUOAE in diabetic children. Effects of 1.0 kHz and 2.0 kHz pure tone stimulation preliminary study. Scand Audiol 2001;30(Suppl 52):126–129
32 Kakarlapudi V, Sawyer R, Staecker H. The effect of diabetes on sensorineural hearing loss. Otol Neurotol 2003;24(03):382–386
33 Lasisi OA, Nwaorgu OGB, Bella AF. Cochleovestibular complications of diabetes mellitus in Ibadan, Nigeria. Int Congr Ser 2003; 1240:1325–1328
34 Gibbin KP, Davis CG, Bhanu TS. A hearing survey in diabetes mellitus. Clin Otolaryngol Allied Sci 1981;6(05):345–350
35 Prado-Barreto VM, Salvatori R, Santos Júnior RC, et al. Hearing status in adult individuals with lifetime, untreated isolated growth hormone deficiency. Otolaryngol Head Neck Surg 2014; 150(03):464–471
36 Muus JS, Weir FW, Kreicher KL, Bowlby DA, Discolo CM, Meyer TA. Hearing loss in children with growth hormone deficiency. Int J Pediatr Otorhinolaryngol 2017;100:107–113
37 Hwang JH, Hsu CJ, Liu TC, Yang WS. Association of plasma adiponectin levels with hearing thresholds in adults. Clin Endocrinol (Oxf) 2011;75(05):614–620
38 Goldstein BJ, Scalia R. Adiponectin: A novel adipokine linking adipocytes and vascular function. J Clin Endocrinol Metab 2004; 89(06):2563–2568
39 Magge SN, Stettler N, Koren D, et al. Adiponectin is associated with favorable lipoprotein profile, independent of BMI and insulin resistance, in adolescents. J Clin Endocrinol Metab 2011;96(05): 1549–1554
40 Frisina ST, Mapes F, Kim S, Frisina DR, Frisina RD. Characterization of hearing loss in aged type II diabetics. Hear Res 2006;211(1-2):103–113
41 Evans MB, Tonini R, Shope CD, et al. Dyslipidemia and auditory function. Otol Neurotol 2006;27(05):609–614
42 Shargorodsky J, Curhan SG, Eavey R, Curhan GC. A prospective study of cardiovascular risk factors and incident hearing loss in men. Laryngoscope 2010;120(09):1887–1891
43 Hwang JH, Wu CC, Hsu CJ, Liu TC, Yang WS. Association of central obesity with the severity and audiometric configurations of age-related hearing impairment. Obesity (Silver Spring) 2009;17(09): 1796–1801
44 Kılıç K, Sakat MS, Çayır A. Evaluation of Hearing in Children with Metabolic Syndrome. Turk Arch Otorhinolaryngol 2018;56(03): 160–165
45 Bener A, Al-Hamaq AOAA, Abdulhadi K, Salahaldin AH, Gansan L. Interaction between diabetes mellitus and hypertension on risk of hearing loss in highly endogamous population. Diabetes Metab Syndr 2017;11(Suppl 1):S45–S51
46 McGaughran JM, Price DA, Kerr BA. Precocious puberty, endometriosis, skeletal anomalies and mild hearing loss: a new autosomal dominant syndrome? Clin Dysmorphol 2001;10 (04):235–239
47 Nishi E, Mizuno S, Nanjo Y, et al. A novel heterozygous MAP2K1 mutation in a patient with Noonan syndrome with multiple lentigines. Am J Med Genet A 2015;167A(02):407–411