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The Importance of Extended High Frequencies in Hearing Evaluation of Pediatric Patients with Type 1 Diabetes

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What is already known on this topic?

Diabetes-induced hearing loss is considered a progressive sensorineural hearing loss with a gradual onset typically occurring at high frequencies (HFs). However, studies investigating extended HFs (EHFs) in pediatric patients with type 1 diabetes (T1D) are limited.

What this study adds?

There was a higher prevalence of hearing loss at EHFs in children with T1D, although the patients did not complain of hearing loss. This finding highlights the need for auditory evaluation of children with T1D to be performed both at the frequency range used in conventional audiometry and at EHFs.

Abstract

Objective: Type 1 diabetes (T1D), one of the most common childhood diseases worldwide, can cause hearing loss through systemic effects. Diabetes-induced hearing loss is considered a progressive sensorineural hearing loss with a gradual onset, typically occurring at high frequencies (HFs). Extended HF (EHF) hearing sensitivity in children with T1D who did not complain of hearing loss was investigated as an early marker for hearing loss at the standard/conventional frequency range of hearing.

Methods: Forty-two children (21 with T1D and 21 healthy controls) were evaluated in a case-control design. Conventional and EHF (14,000, 16,000, and 18,000 Hz) audiometry were performed. The diabetes group underwent routine blood biochemistry and glycated hemoglobin A1c measurements. The data were analyzed by the Student's t-test, Mann-Whitney U test, chi-square test, and logistic regression analysis.

Results: The mean hearing thresholds were significantly higher ($p < 0.05$) in the diabetes group than in controls at 500, 2,000, 4,000, and 8,000 Hz [all < 15 decibel hearing level (dB HL)]. The number of ears with thresholds > 15 dB HL at 14,000-18,000 Hz but ≤ 15 dB HL at 500-4,000 Hz was significantly higher in the diabetes group than in the control group ($p = 0.049$).

Conclusion: Children with diabetes showed normal hearing thresholds within the conventional audiometric frequency range but they had higher hearing thresholds during EHF audiometry when compared with controls. Audiometry in these children should be performed using frequencies above 8,000 Hz combined with the conventional frequency range. EHF audiometry may be an effective method for identifying subclinical hearing loss in children with diabetes. Thus, diabetic children with an EHF mean hearing threshold above 15 dB HL should be monitored more closely in terms of blood glucose regulation to prevent diabetes-related hearing loss at the conventional frequency range.

Keywords: Type 1 diabetes, children, hearing, extended high-frequency audiometry, hearing impairment

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Introduction

Type 1 diabetes (T1D) is one of the most prevalent long-term diseases of childhood worldwide. The young population with documented T1D in Turkey represents ~3% of the approximately 500,000 T1D cases worldwide (1). Diabetes is a chronic disorder of carbohydrate metabolism induced by absolute or relative insulin deficiency that impedes several organ systems. The multiorgan effects of diabetes include microangiopathy and/or neuropathy throughout the disease duration (2). Hearing impairment and loss of balance due to neuropathy and angiopathy are well-known clinical manifestations in both type 1 and type 2 diabetes (3,4,5,6). Neuropathy, vascular thrombosis, and arteriolar spasm, gradually developing in patients with diabetes, can cause loss of hearing (3,5,6,7). Diabetes-induced hearing impairment is characterized by a moderate loss of sensorineural hearing involving a lack of perception of high-frequency sounds; it affects both ears and leads to progressive hearing loss (5,6,8).

Although the underlying mechanism remains controversial, it is suggested that microangiopathy could lead to hearing loss in diabetic patients (9,10). Another potential mechanism involves changes in glucose metabolism (11). It is assumed that excess free oxygen radicals, formed because of nonenzymatic glycation in individuals with diabetes, may cause toxicity in the outer hair cells of the ears, eventually leading to hearing loss.

Previous studies on the presence, pattern, and severity of hearing loss and its relationship with metabolic control in patients with diabetes were inconclusive (12) and mostly involved adults with type 2 diabetes. To date, only a limited number of studies have documented marked hearing loss in young patients with T1D, particularly children with a relatively short disease duration (13). Hearing loss in adult patients with diabetes could be related to aging rather than solely to diabetes-induced neurovascular degeneration, whereas hearing loss in children with T1D most likely reflects the primary effects of diabetes (14). In their 2017 meta-analysis, Teng et al. (15) revealed a relationship between T1D and auditory dysfunction and reported that although hearing loss is mild and subclinical in T1D, the probability of hearing loss is higher compared with that in controls.

A young, healthy individual can often hear pure tones up to approximately 20 kHz. However, clinical audiometry, the gold standard for detecting hearing loss, typically measures tonal sensitivity up to 8 kHz (16). This suggests that achieving a normal pure-tone hearing threshold on an audiogram does not mean that there is no pathology in the cochlea or the central auditory nervous system (17). Therefore, conventional pure-tone audiometry should be complemented by extended high-frequency (EHF) (> 8 kHz) audiometry (17,18,19) to achieve an accurate diagnosis for people with a normal conventional audiogram who have listening difficulties or people with history of noise exposure and/or disorders that affect basal regions of the cochlea, such as T1D. This type of audiometry may be useful in the early diagnosis of hearing loss in certain situations, such as the ototoxic effect of cisplatin-based treatment, noise exposure, or oral misunderstanding, especially in noisy environments (20) and with T1D. EHF hearing is important for our understanding of speech in noise (17), potentially affecting academic success in school-age children. Therefore, EHF audiometry could also be a useful tool for the early diagnosis of hearing impairment in childhood (18,19). To date, only one study has investigated EHFs in children with T1D (21). The main difference between this and the present study is identification of diabetic children with subclinical hearing loss by using different frequency ranges, especially EHFs. Thus, we tested the diagnostic value of EHF audiometry in diabetic children.

Methods

This study was approved by the Ethics Committee of Trakya University and was conducted as per the tenets of the Declaration of Helsinki (decision no: 07/08, date: 13.04.2020). Informed consent was obtained from all subjects and their parents.

Participants

Forty-two children (84 ears from 21 patients with T1D and 21 healthy controls) were included. All subjects were aged 5-18 years and the study had a case-control design. Diabetic children were recruited from the pediatric endocrinology department, and the control group comprised healthy children who were referred to our center for an auditory evaluation for a school/course application. Our primary inclusion criterion for children in both groups was the absence of complaints of hearing loss. The exclusion criteria were any middle ear pathology, such as acute/chronic otitis media and otosclerosis, or history of middle ear surgery, ototoxic medication use, known family history of hearing loss, severe febrile illness, or previous head trauma.

A detailed pediatric and ear-nose-throat (ENT) physical examination was performed in both groups. Weight and height were measured and used to calculate body mass index (BMI) using the standard formula. Systolic/diastolic blood pressure (BP) was measured, and individuals with BP in the 95th percentile or higher were considered hypertensive

(22). For the diabetes group, we collected baseline venous blood samples after a 12-hour fasting period to determine the levels of fasting blood glucose, urea nitrogen, creatinine, total cholesterol, triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and glycated hemoglobin (HbA1c). HbA1c values under 7.5% were considered to indicate good metabolic control, values of 7.5-9.0% indicated moderate metabolic control, and those above 9% indicated poor metabolic control (23). Dyslipidemia was diagnosed if one or more of the following parameters were met: LDL-C >2.6 mmol/L, HDL-C <1.1 mmol/L or TG >1.5 mmol/L (24). Microalbuminuria was defined as an albumin excretion rate of 30-300 mg/24 hours in 2 out of 3 early morning urine samples within 3-6 months of the first positive urine test (25). Tests were performed for vibration, pressure sensation, and proprioception to screen for diabetic polyneuropathy. A retinal examination was performed by an ophthalmologist in the diabetes group.

Audiological Evaluations

Otoscopic examination of all children was performed by the same ENT physician. Children with bilaterally normal otoscopic examination were included in the study, and audiological evaluations were made. The same audiologist performed the audiological tests in all children, which included pure-tone audiometry and tympanometry. Tympanometry and acoustic reflex testing were performed using an Interacoustics AZ26 (Interacoustics, Assens, Denmark) impedance audiometer. In immittance measurements, middle ear pressures and acoustic reflexes were measured with a probe tone of 226 Hz and an intensity of 85 dB sound pressure level. In the automatic evaluation, pressure between +200 daPa and -400 daPa was applied, and tympanogram types of all children were obtained. Both ipsilateral acoustic reflex and contralateral stapes reflex thresholds were evaluated as present/absent. Pure-tone audiometry was performed in a sound-treated booth using an Interacoustics AC40 (Interacoustics, Assens, Denmark) audiometer and Telephonics TDH-39P (Telephonics, USA) earphones. Children with normal tympanic membranes, type A tympanogram [Jerger et al.'s (26) classification], ipsilateral and contralateral stapes reflexes (at 1 kHz) within normal limits, and without conductive hearing loss on audiogram were included in the study, as long as they did not have middle ear pathology. Air and bone conduction were tested at frequencies of 250-8,000 Hz and 250-4,000 Hz, respectively. An air-bone gap over 10 dB HL is defined as conductive hearing loss. Children with an air-bone gap at any frequency above 10 dB HL were excluded. Children with an airway threshold average above 20 dB HL at speech frequencies (SF) of 500-4,000 Hz in the audiogram were also excluded from the study. In addition to using the 250-8,000 Hz frequency range in conventional audiometry, we performed auditory evaluations at EHFs of 14,000, 16,000, and 18,000 Hz in all children included in the study. Koss R/80 (Koss Co., USA) earphones were used for high-frequency audiometry. Pure-tone audiometry measurements were first performed at the conventional frequency range, followed by the EHF range. The ascending method was used to obtain the pure-tone audiometry thresholds (27). The step size used to measure the threshold was 5 dB. This step size provides the opportunity to obtain the hearing threshold more quickly and to control the accuracy of the threshold in most children with normal hearing (28). Special care was taken with each of the young participants as they could potentially become bored, and they were given breaks if necessary. Patients who recorded thresholds above 15 dB HL in the conventional pure-tone audiogram were considered to have hearing loss (18,19). Based on previous studies, we also performed statistical evaluations using a threshold value of 15 dB HL for EHFs (18,19). While analyzing the hearing measurements, the threshold values for each measured frequency and the pure-tone average threshold values of some frequency ranges (500-4,000 Hz as the human SF range; 4,000-8,000 Hz as the high frequency (HF) range; 14,000-18,000 Hz as the EHF range) were computed and used to reveal the exact frequency range that could be more predictive as a diagnostic approach.

Whether there was sensorineural hearing loss at the EHF in the diabetes group compared with the control group was investigated. The age at the time of diagnosis, duration of disease, HbA1c values, and data on microalbuminuria, dyslipidemia, retinopathy, and neuropathy were evaluated to investigate whether the potential sensorineural hearing loss in the diabetes group was related to metabolic control of T1D.

Statistical Analysis

The Shapiro-Wilk test was used to evaluate the normality of distribution of quantitative variables. Mean ± standard deviation was used as descriptive statistics for normally distributed quantitative data, median (minimum-maximum) values were used for non-normally distributed quantitative data, and numbers (%) were used for categorical variables.

The sample size was calculated as 36 ears for each group based on an effect size of 0.873 at 16,000 Hz frequency (21) with an alpha level of 5% and power of 95%. Considering the possibility of missing data, we included 42 ears in each group.

The Student's t-test was used to compare normally distributed quantitative data (age and BMI) between the diabetes and control groups and the Mann-Whitney U test to compare non-normally distributed quantitative hearing thresholds and HbA1c (%) between groups (healthy controls vs diabetes, disease duration <5 vs. ≥5 years). Comparison of mean hearing thresholds among frequency ranges was done using the Freidman test. The Pearson chi-square, Yates correction, and Fisher's exact tests were used as appropriate to compare categorical data (hearing thresholds >15 vs. ≤15 dB HL) between the groups. Potential confounders were analyzed by logistic regression analysis with the enter method. A value of $p < 0.05$ was considered statistically significant. Statistical analysis was done with Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM SPSS Statistics for Windows, version 20.0. Armonk, NY: IBM Corp.).

Results

The general characteristics of the study population are given in Table 1. Both groups were similar in terms of age, gender distribution, and BMI.

Table 2 summarizes the audiometric test results. When the mean differences in frequency-specific hearing thresholds were analyzed after performing the auditory evaluations using both conventional and EHF methods, it was found that

Table 1. General characteristics of study groups

	Diabetes (n = 42 ears)	Control (n = 42 ears)	p
Age, years	11.9 ± 2.6	11.3 ± 2.6	0.448
Sex (male/female)	22/20	20/22	1.000
BMI, kg/m^2	19.1 ± 3.1	18.4 ± 2.0	0.302
BMI SDS	-0.030 ± 1.105	-0.162 ± 0.721	0.529
HbA1c	9.22 ± 1.56	-	-
Microalbuminuria, yes	4 (9.5%)	-	-
Dyslipidemia, yes	16 (38.1%)	-	-
Disease duration, years	5.19 ± 2.78	-	-
Mean age at the time of diagnosis, years	6.76 ± 3.17	-	-

BMI: body mass index; BMI SDS: BMI standard deviation score, HbA1c: glycated hemoglobin

Table 2. Hearing thresholds (dB HL) of ears and the number of ears with a threshold value above 15 dB HL at each frequency in the diabetes and control groups

Frequency (Hz)	dB HL	Diabetes (n = 42 ears)	Control (n = 42 ears)	p
250	Mean ± SD	11.6 ± 4.2	11.6 ± 5.0	0.924
	>15	5 (11.9%)	7 (16.7%)	0.755
500	Mean ± SD	12.0 ± 4.8	9.0 ± 3.1	**0.002**
	>15	4 (9.5%)	0 (0.0%)	0.116
1,000	Mean ± SD	7.3 ± 4.8	6.0 ± 2.3	0.327
	>15	4 (9.5%)	0 (0.0%)	0.116
2,000	Mean ± SD	8.0 ± 4.5	5.4 ± 2.1	**<0.001**
	>15	2 (4.8%)	0 (0.0%)	0.494
4,000	Mean ± SD	8.9 ± 5.2	5.5 ± 1.6	**<0.001**
	>15	3 (7.1%)	0 (0.0%)	0.241
8,000	Mean ± SD	11.9 ± 5.6	6.6 ± 3.0	**<0.001**
	>15	7 (16.7%)	0 (0.0%)	**0.012**
14,000	Mean ± SD	8.5 ± 12.9	7.2 ± 5.4	0.081
	>15	6 (14.3%)	3 (7.1%)	0.483
16,000	Mean ± SD	11.0 ± 15.0	8.5 ± 7.3	0.103
	>15	11 (26.2%)	6 (14.3%)	0.277
18,000	Mean ± SD	10.3 ± 11.0	7.2 ± 5.0	0.993
	>15	12 (28.6%)	2 (4.8%)	**0.008**

dB HL: decibel hearing level, SD: standard deviation.
n (%)

the diabetes group had higher mean hearing thresholds than the control group at all frequencies except 250 Hz; however, all the children's mean hearing thresholds were under 15 dB HL. The mean thresholds of both groups were equal at a frequency of 250 Hz. The higher mean hearing thresholds in the diabetes group were statistically significant only at 500, 2,000, 4,000, and 8,000 Hz (Table 2). Table 2 also shows the number of ears with hearing thresholds above 15 dB HL at each frequency in the diabetes and control groups. The number of ears with a threshold value above 15 dB HL was significantly higher in the diabetes group than in the control group at frequency ranges of 8,000 Hz ($p = 0.012$), 18,000 Hz ($p = 0.008$), and 14,000-18,000 Hz ($p = 0.023$, Tables 2 and 3). There was no significant between-group difference in the number of ears with mean hearing threshold values above 15 dB HL at the 500-4,000 Hz frequency range ($p = 0.241$, Table 3). Although there was no ear with a mean hearing threshold value above 15 dB HL at this frequency range in the control group, there were three ears with threshold values above 15 dB HL in the diabetes group, all of which were ≤20 dB HL (Table 3).

Table 3 shows hearing thresholds and the number of ears with a threshold value above 15 dB HL at different frequency ranges. It was found that the mean hearing thresholds at the SF (500-4,000 Hz), HF (4,000-8,000 Hz), and EHF (14,000-18,000 Hz) ranges were higher in the diabetes group than in the control group, but they were statistically significant only in the SF and HF ranges.

Table 4 shows the number of ears with a normal hearing threshold (≤15 dB HL) at the SF range but above 15 dB HL at the HF and EHF ranges in both the diabetes and control groups. According to conventional SF test results, 39 ears in the diabetes group and 42 ears in the control group were within normal limits. However, extending the audiometry to EHF in these healthy ears revealed that 10 (25%) ears in the diabetes group and 3 (7%) ears in the control group had subclinical hearing loss. Additionally, mean hearing thresholds at the EHF range (25.7 ± 9.3 dB HL) were significantly higher in the diabetes group (n = 10) compared with the mean hearing threshold at the SF range (8.8 ± 2.8 dB HL; $p = 0.005$). In the control group (n = 3), there was no significant difference between mean hearing thresholds at the EHF (22.2 ± 6.9 dB HL) and those at the SF range (10.8 ± 4.0 dB HL; $p = 0.109$).

To evaluate the role of age in the hearing thresholds of children with T1D, the correlation of hearing thresholds at each frequency with age was investigated. A significant positive correlation was found between age and threshold values at 8,000 Hz in the diabetes group ($r = 0.460$; $p = 0.036$). There was no significant correlation between mean hearing threshold and age at other frequencies. In the control group, there was no significant correlation between age and hearing thresholds at any frequency (data not shown).

Table 5 gives a comparison of the median hearing thresholds of patients with T1D at each frequency based on disease duration. In the diabetes group, the mean duration of disease for T1D was 5.19 ± 2.78 years. Mean hearing thresholds at 250, 500, 2,000, 4,000, 500-4,000, and 4,000-8,000 Hz were significantly higher in patients with a disease duration

Table 3. Hearing thresholds (dB HL) and the number of ears with a threshold value above 15 dB HL of ears at different frequency ranges in diabetes and control groups

Pure-tone audiometry	dB HL	Diabetes (n = 42 ears)	Control (n = 42 ears)	p
Speech frequency (500-4,000 Hz)	Mean ± SD	9.1 ± 3.7	6.5 ± 1.8	**< 0.001**
	> 15, n (%)	3 (7.1%)	0 (0%)	0.241
High frequency (4,000-8,000 Hz)	Mean ± SD	10.4 ± 4.9	6.1 ± 2.0	**< 0.001**
	> 15, n (%)	5 (11.9%)	0 (0%)	0.055
Extended high frequency (14,000-18,000 Hz)	Mean ± SD	10.0 ± 12.1	7.6 ± 5.2	0.385
	> 15, n (%)	12 (28.6%)	3 (7.1%)	**0.023**

dB HL: decibel hearing level, SD: standard deviation

Table 4. The number of ears with normal hearing threshold (≤15 dB HL) at speech frequency range but above 15 dB HL at high and EHF ranges

Diabetes (n = 39)		Hearing loss at high frequency (4,000-8,000 Hz) (> 15 dB HL)			Hearing loss at EHF (14,000-18,000 Hz) (> 15 dB HL)		
		Control (n = 42)	p	Diabetes (n = 39)	Control (n = 42)	p	
Speech frequency (500-4,000 Hz)	≤15 dB HL	2 (5.1%)	0 (0%)	0.229	10 (25.6%)	3 (7.1%)	**0.049**

dB HL: decibel hearing level, EHF: extended high frequency.
n (%)

of ≥5 years compared with those with a disease duration of <5 years (Table 5).

The mean HbA1c value of all diabetic children included in the study group was 9.22 ± 1.56%. A subgroup analysis was performed based on HbA1c and compared the HbA1c values between patients with or without hearing loss at all tested frequencies (Table 6). It was found that those with thresholds above 15 dB HL at 2,000 and 4,000 Hz also had significantly higher HbA1c ($p < 0.05$). Among the patients with a normal hearing result in the conventional SF range, the mean HbA1c value was higher in patients with a hearing threshold >15 dB HL at the EHF range compared with patients with a hearing threshold ≤15 dB HL at the EHF range (9.47% vs. 8.94%, respectively). However, this difference failed to reach significance ($p = 0.421$). In addition, a correlation analysis was performed between HbA1c and mean hearing threshold at different frequency ranges. No significant correlation was identified (Supplementary Table 1).

When patients were grouped according to HbA1c values (see Methods section), the frequency of hearing thresholds above 15 dB HL at 500 Hz was significantly higher in the group with moderate metabolic control than in the good and poor control groups ($p = 0.005$). There was no significant difference at other frequencies. The percentage of diabetic patients with good, moderate, or poor metabolic control was compared among the hearing threshold groups at different frequency ranges (Figure 1; $p > 0.05$).

Table 5. Comparison of the median hearing thresholds (dB HL) of patients with type 1 diabetes at each frequency based on disease duration

Frequency	Disease duration		p[a]
	<5 years (n = 11)	≥5 years (n = 10)	
250 Hz	10 (5-15)	15 (10-20)	**0.045**
500 Hz	10 (5-15)	15 (10-25)	**0.005**
1000 Hz	5 (5-10)	5 (5-20)	0.690
2000 Hz	5 (5-5)	7.5 (5-20)	**0.009**
4000 Hz	5 (5-10)	10 (5-25)	**0.014**
8000 Hz	10 (5-20)	12.5 (10-25)	0.081
14000 Hz	5 (0-50)	0 (0-45)	0.681
16000 Hz	5 (0-55)	2.5 (0-40)	0.556
18000 Hz	10 (0-30)	10 (0-30)	0.856
500-4000 Hz	6.25 (5.25-7.5)	10 (6.25-18.75)	**0.002**
4000-8000 Hz	7.5 (5-15)	10 (7.5-25.5)	**0.017**
14000-18000 Hz	6.67 (0-45)	6.67 (0-38.3)	0.774

dB HL: decibel hearing level.
[a]Mann-Whitney U test, median (minimum-maximum).

Table 6. Comparison of the HbA1c values of patients with type 1 diabetes based on their hearing thresholds at each frequency

Frequency	Hearing ≤15 dB HL	Hearing >15 dB HL	p[a]
250 Hz	9.2 (6.9-12.6)	8.4 (8.0-12.6)	0.938
500 Hz	9.2 (6.9-12.6)	8.4 (8.0-8.5)	0.230
1000 Hz	9.2 (6.9-12.6)	8.4 (8.0-12.6)	0.864
2000 Hz	9.05 (6.9-11.8)	12.6 (12.6-12.6)	**0.018**
4000 Hz	8.9 (6.9-11.8)	12.6 (9.6-12.6)	**0.024**
8000 Hz	9.2 (6.9-11.8)	9.3 (8.0-12.6)	0.457
14000 Hz	9.05 (6.9-12.6)	10.8 (8.0-12.6)	0.098
16000 Hz	8.9 (6.9-11.8)	11.0 (7.3-12.6)	0.063
18000 Hz	9.2 (6.9-11.8)	9.45 (7.3-12.6)	0.419
500-4000 Hz	9.2 (6.9-11.8)	12.6 (8.4-12.6)	0.096
4000-8000 Hz	9.2 (6.9-11.8)	9.6 (8.1-12.6)	0.243
14000-18000 Hz	9.05 (6.9-11.8)	10.4 (7.3-12.6)	0.112

HbA1c: glycated hemoglobin, dB HL: decibel hearing level.
[a]Mann-Whitney U test, median (minimum-maximum).

In terms of mean hearing threshold ≤15 dB HL or >15 dB HL at each frequency measured, patients with and without microalbuminuria and dyslipidemia were comparable. Presence or absence of microalbuminuria and/or dyslipidemia was not a distinguishing factor between the patients who had hearing loss at different frequency ranges (Figures 2 and 3; p>0.05). There were no patients with retinopathy or neuropathy in the diabetes group.

The effect of potential confounders (age, BMI, disease duration, and HbA1c) on hearing loss at different frequency ranges (SF, HF, and EHF) of pure-tone audiometry was analyzed by logistic regression, and no significant effect on hearing loss was found (Table 7).

Discussion

The findings of this study imply that using EHFs during audiometric evaluation in diabetic children may reveal hearing impairment, which in turn may be evidence of

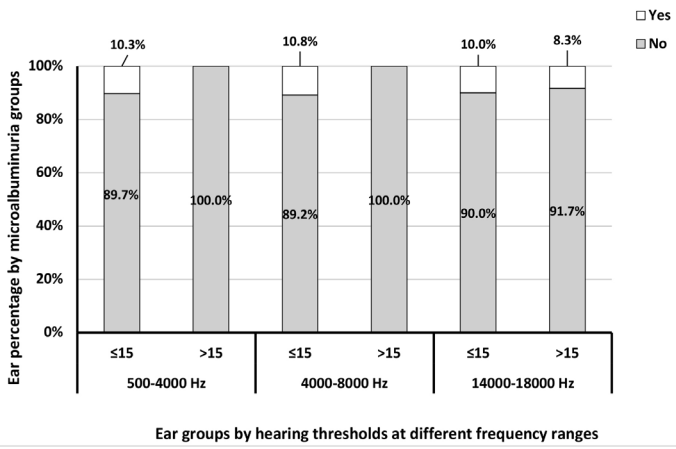

Figure 2. Distribution of microalbuminuria groups based on diagnostic criteria among ears with a hearing threshold >15 or ≤15 dB HL at different frequency ranges

dB HL: decibel hearing level, Yes: microalbuminuria present, No: microalbuminuria absent

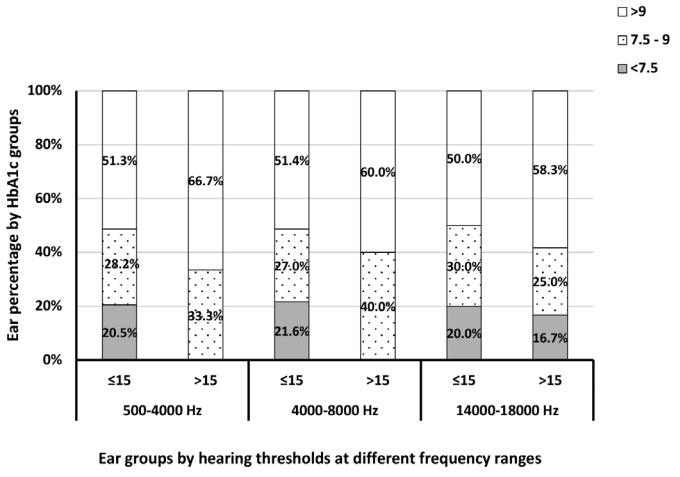

Figure 1. Distribution of metabolic control groups based on HbA1c levels (1: <7.5%; 2: 7.5-9%; 3: >9%) among ears with a hearing threshold >15 or ≤15 dB HL at different frequency ranges

HbA1c: glycated hemoglobin, dB HL: decibel hearing level

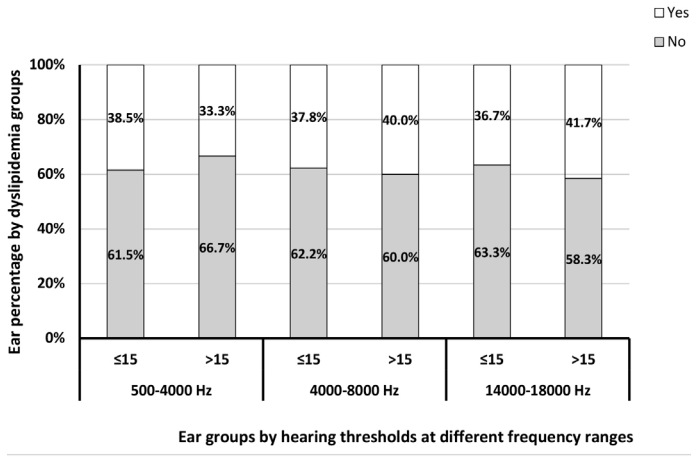

Figure 3. Distribution of dyslipidemia groups based on diagnostic criteria among ears with a hearing threshold >15 or ≤15 dB HL at different frequency ranges

dB HL: decibel hearing level, Yes: dyslipidemia present, No: dyslipidemia absent

Table 7. The effect of potential confounders on hearing loss (>15 dB HL) at different frequency ranges (speech frequency, high frequency, and EHF) of pure-tone audiometry by logistic regression

	Hearing loss at speech frequency			Hearing loss at high frequency			Hearing loss at EHF		
	Wald statistics	p	OR (95% CI)	Wald statistics	p	OR (95% CI)	Wald statistics	p	OR (95% CI)
Age, years	1.07	0.302	0.57 (0.20-1.66)	0.93	0.334	0.78 (0.47-1.29)	2.53	0.112	0.75 (0.52-1.07)
BMI (kg/m^2)	1.24	0.266	0.10 (0-5.92)	0.73	0.392	1.16 (0.82-1.65)	1.84	0.175	0.77 (0.53-1.12)
Disease duration, years	1.21	0.271	0.48 (0.13-1.78)	0.01	0.934	1.02 (0.64-1.63)	1.19	0.275	1.24 (0.85-1.81)
HbA1c (%)	0.64	0.424	1.64 (0.49-5.49)	0.63	0.427	1.42 (0.60-3.40)	0.89	0.345	1.31 (0.75-2.28)

OR: odds ratio, CI: confidence interval, BMI: body mass index, HbA1c: glycated hemoglobin, dB HL: decibel hearing level, EHF: extended high frequency

early changes related to hearing loss. Hearing impairment in patients with diabetes has been investigated for several years but previous studies on the presence, pattern, and severity of hearing loss and its relationship with metabolic control have been inconclusive (12). Diabetes-induced hearing loss is considered a progressive sensorineural type of hearing loss with a gradual onset typically occurring at HFs (5,6,8). A higher prevalence of hearing loss in EHF was found in the present study, although there was no complaint of hearing loss in the children with T1D. Diabetic children with an EHF mean hearing threshold above 15 dB HL should be monitored more closely in terms of regulation of blood glucose levels to prevent diabetes-related hearing loss.

In conventional audiometry, the air conduction pathway is examined at 250-8,000 Hz and the bone conduction pathway at 500-4,000 Hz. In our study, the mean hearing thresholds of patients with T1D were higher than those of the healthy controls. At frequencies of 500, 2,000, 4,000, and 8,000 Hz, this difference was statistically significant but the mean hearing threshold was not higher than 15 dB HL at any frequency. Among diabetic patients, the number of ears with a normal mean hearing threshold (≤15 dB HL) at the SF range but a mean hearing threshold above 15 dB HL at the EHF range was significantly higher compared with that in the healthy controls. Although the increase in mean hearing thresholds at the EHF range was not significant in the diabetes group compared with that in the control group, the fact that the number of ears with a mean hearing threshold ≤15 dB HL at the SF range but >15 dB HL at the EHF range was significantly higher in patients with T1D suggests that these frequencies should be further investigated. These ears might be overlooked when only conventional audiometry frequencies are considered while analyzing EHFs could contribute to early recognition of the pathogenetic process already initiated in the inner ear in children with T1D.

Most previous studies on T1D and hearing used ≤8,000 Hz pure-tone audiometry. Four studies used >8,000 Hz pure-tone audiometry. Of these, only one was performed in the pediatric age group (21), and the mean age of cases in the other three studies was over 20 years (29,30,31). Abd El Dayem et al. (21) performed pure-tone audiometry (250-18,000 Hz) and transient-evoked otoacoustic emission (TEOAE). Similar to our study, the thresholds in patients with diabetes were higher than those in the controls at all frequencies. However, significantly higher hearing thresholds were recorded at 8,000, 16,000, 17,000, and 18,000 Hz in the right ear and at 4,000, 8,000, 16,000, 17,000, and 18,000 Hz in the left ear. They found no significant difference between patients with diabetes and controls at low and medium frequencies ≤4,000 Hz. Their findings show significant decreases in the signal/noise ratio in TEOAE at 4,000 Hz in the right ear and at 1,000, 1,500, and 4,000 Hz in the left ear in patients compared with controls, suggesting cochlear pathology. The authors concluded that audiometric evaluation at HF and EHF could help detect underlying hearing impairments in children with diabetes more effectively than conventional audiometry and our results support this finding. In our study, in frequency-based comparisons, we found a significant increase in thresholds of diabetic children at 500, 2,000, 4,000, and 8,000 Hz, but we did not detect a significant increase in EHF. However, the mean hearing values at each frequency in all of our cases were less than 15 dB HL. We found a higher prevalence of hearing loss in EHF in type 1 diabetic children with clinically normal hearing. We paid particular attention to the fact that all patients included in the study did not have hearing loss complaints. In the study of Abd El Dayem et al. (21), the average hearing thresholds were higher than in ours. The lower mean age and mean HbA1c value of our diabetic patients may have contributed to this difference.

Two other studies (30,31) investigated auditory involvement in adults with T1D. Dabrowski et al. (30) reported that the mean hearing thresholds at frequencies of 3,000, 4,000, 6,000, 8,000, and 12,000 Hz were significantly higher in patients with T1D. Malucelli et al. (31) also found that the mean hearing values of both ears at 250, 500, 9,000, 10,000, 11,200, 12,500, 14,000, and 16,000 Hz in the patient group were significantly higher than in the control group. They also detected thresholds of under 20 dB at frequencies ≤10,000 Hz and above 20 dB at frequencies ≥10,000 Hz. Similar to our findings, Dabrowski et al. (30) found that all mean thresholds were under 20 dB. Their report of higher mean hearing thresholds could be attributed to the fact that the mean age of patients in our study was 11.3 ± 2.6 years, whereas both abovementioned studies enrolled adults aged over 25 years. In 1980, Osterhammel and Christau (29) evaluated high-frequency hearing and stapedius reflex thresholds at 250-20,000 Hz in 61 patients with insulin-dependent diabetes, aged 20-50 years, and compared their results with normative data of nondiabetic matched controls. They reported that, unlike in our study, there was no significant difference between the two groups in the hearing and stapedius reflex thresholds.

Two meta-analyses revealed the relationship between T1D and auditory dysfunction (14,15). In one study, the prevalence of hearing loss was higher in patients with diabetes compared with controls, even if the hearing impairment was mild and subclinical (15). The other study reported that hearing loss indicated subclinical microvascular damage and should be recognized as equivalent to subclinical neuropathy,

retinopathy, and nephropathy, which can require a stringent treatment/management regimen to prevent late disease complications (14).

Aiming to evaluate functional hearing and general communication skills in school-age children with T1D, Rance et al. (32) investigated both cochlear and auditory neural function using auditory brainstem response (ABR), pure-tone audiometry at 250-8,000 Hz, otoacoustic emissions (OAEs), and behavioral testing techniques. Although the hearing value was ≤15 dB in both groups, the hearing thresholds of the patients were significantly higher than those of the healthy controls. Furthermore, these authors reported lower mean response amplitudes in distortion product OAE (DPOAE) and decreased V-wave amplitudes and prolonged I-V waves in the ABR of the patients. Additionally, their patients had impaired bilateral speech perception in noisy environments, and their perceptual ability and degree of neural deterioration in the auditory brainstem were correlated. The authors concluded that a functional hearing impairment that is severe enough to limit communication and threaten academic progress is common in school-age children with T1D and that standard audiometry was not an effective screening method in their population. We conclude that EHFs should be included in the standard follow-up regimens of these children and auditory screening tests in schools.

The relationship between hearing, duration of disease, and other metabolic changes in patients with T1D remains inconclusive. Comparison of diabetic patients with a disease duration of greater than versus less than 5 years revealed that hearing thresholds were higher in the group with longer disease duration. Grouping patients based on HbA1c levels enabled additional comparisons among patients with various metabolic control. As indirect evidence from Figure 1, we suggest that the presence of patients with good metabolic control in EHF tests and absence of patients with good metabolic control in conventional frequencies could indicate the sensitivity of using EHF to detect hearing loss at early stages. Abd El Dayem et al. (21) found that the rate of failed OAE in patients with a disease duration of more than 10 years was significantly higher than those with a disease duration of less than 10 years. However, they did not find a significant relationship between hearing, disease duration, and HbA1c at EHFs (16,000, 17,000, and 18,000 Hz). Dąbrowski et al. (30) reported that diabetes duration and metabolic control were not related to hearing thresholds and ABR results. Rance et al. (32) found no relationship between the mean hearing level, age at the time of disease onset, duration of disease, and HbA1c levels. However, Mujica-Mota et al. (14) found that the duration of diabetes contributed markedly to the development of hearing loss and concluded that the relative risk increases over time. The fact that the number, mean age, and duration of disease of diabetic cases were higher in the studies included in Mujica-Mota et al.'s (14) meta-analysis than in other studies may explain this difference.

Study Limitations

The most important limitation of our study was our inability to perform other electrophysiological tests (OAE, ABR) to evaluate hearing. Another limitation could be lack of other extended frequencies, such as 10 and 12.5 kHz, which would provide additional information. The relationship between the metabolic control of T1D and hearing loss remains controversial, and future studies using electrophysiological tests in addition to pure-tone audiometry on a greater number of pediatric patients could contribute significantly to the current literature. Although the number of patients was sufficient in the power analysis for the study, the number was insufficient for the subgroup analysis. If more patients had been included, the result might be more robust.

Conclusion

In conclusion, our findings suggest that the auditory evaluation of children with T1D should be performed both at the frequency range used in conventional audiometry and at EHFs, although larger-scale studies will be required in the future to support and confirm these results. Pure-tone audiometers are more widely used, more accessible, and cheaper. Therefore, we believe that EHF audiometric evaluation has potential for early detection of subclinical hearing impairment in children with T1D. Early detection of impaired hearing at higher frequencies could be an early and useful warning sign that will enable intervention which may aid in preservation of hearing in these children. Diabetic children with an EHF mean hearing threshold above 15 dB HL should be monitored more closely in terms of regulation of blood glucose levels to prevent diabetes-related hearing loss. Therefore, this approach combined with increased metabolic control could allow for an improved disease process and a more stable academic life for these children.

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Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Trakya University and was conducted as per the tenets of the Declaration of Helsinki (decision no: 07/08, date: 13.04.2020).

Informed Consent: Informed consent was obtained from all subjects and their parents.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Selis Gülseven Güven, Çiğdem Binay, Concept: Selis Gülseven Güven, Design: Selis Gülseven Güven, Data Collection or Processing: Selis Gülseven Güven, Çiğdem Binay, Analysis or Interpretation: Selis Gülseven Güven, Çiğdem Binay, Literature Search: Selis Gülseven Güven, Çiğdem Binay, Writing: Selis Gülseven Güven, Çiğdem Binay.

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