

Impact of different modifiable factors on hearing function in type 1 and type 2 diabetic subjects. A preliminary study

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Abstract

Introduction and objective: Hearing impairment in diabetic subjects is more prevalent than in the general population. Ageing, noise exposure and smoking are known as risk factors of hearing loss. The aim of this study was to assess whether other factors, such as HbA_{1c}, blood pressure, serum lipids and BMI have an impact on hearing function among relatively young diabetic subjects.

Materials and Methods: 58 patients, 31 with type 1 diabetes and 27 with type 2 diabetes, aged < 45 years, with diabetes duration < 10 years and without overt hearing impairment were included. In all subjects, vital signs, laboratory tests, pure-tone audiometry and transient-evoked otoacoustic emissions (TEOAE) were evaluated.

Results: Hearing impairment was revealed in 20 subjects. This group had a lower HDL-cholesterol level compared with normal hearing patients (44.2 mg/dl vs. 57.6 mg/dl, $p=0.007$). Absence of otoacoustic emissions was diagnosed in 16 subjects. These patients also had a lower HDL-cholesterol level compared with subjects with TEOAE present (45.4 mg/dl vs. 55.2 mg/dl, $p=0.018$). Hearing threshold was inversely correlated with HDL-cholesterol level, and positively correlated with triglycerides. Patients with HDL-cholesterol level ≥ 50 mg/dl had lower hearing threshold at frequencies 0.5–12 kHz, as well as higher TEOAE amplitude. Subjects with triglycerides above median had a higher hearing threshold at frequencies 0.5–12 kHz, as well as lower TEOAE amplitude. Patients with elevated BMI (≥ 25 kg/m²) had a higher hearing threshold at frequencies 2–12 kHz, as well as lower TEOAE amplitude.

Conclusions: Hearing impairment is frequent among relatively young diabetic subjects. The presented study reveals that factors like HDL-cholesterol, triglycerides, and BMI may affect hearing function in this group.

Key words

diabetes mellitus, hearing impairment, pure-tone audiometry, otoacoustic emissions, risk factors

INTRODUCTION

The sense of hearing, together with the sense of sight, are the most important tools of social communication. Hearing gradually deteriorates during the ageing process [1]. Occupational noise exposure, smoking and BMI are well recognized risk factors for age-related hearing loss [2]. Diabetes is also associated with auditory organ dysfunction. Prevalence of hearing impairment among diabetic subjects is roughly doubled when compared with the general population [3]. Impaired hearing and decreased otoacoustic emissions amplitude were found among people with type 1 and type 2 diabetes [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19]. In a population drawn from the National Health and Nutrition Examination Survey (NHANES), among risk factors for hearing impairment in diabetes, low HDL-cholesterol, coronary heart disease and peripheral neuropathy are pointed out, while no association between hearing impairment and glycaemic control, time from diagnosis, and type of anti-diabetic medication were found [20]. However, the list of factors that may have an impact on auditory organ function is not yet complete. In the study by Duck et al., hypertension appeared to increase the hearing thresholds

among diabetic subjects [21]. On the contrary, in an earlier work by Jørgensen & Buch, such a relationship was not observed [22]. The correlation between lipid abnormalities and otoacoustic emission alterations among diabetic subjects was demonstrated in the study by Erdem et al. [23]. These findings indicate that several different factors may have an impact on hearing in diabetes.

The hearing function can be assessed using several audiological tests. The pure-tone audiometry is the most common test used to evaluate hearing sensitivity. Hearing thresholds are assessed at different frequencies and are displayed as an audiogram. This test reflects the function of both the peripheral and central auditory pathways [24]. Another frequently used test is evaluation of otoacoustic emissions (OAEs), used to determine cochlear status, especially outer hair cells (OHC) function. The cochlear response is evoked by a click or pure-tone stimulus and its amplitude is measured in dB. The higher the OAE's amplitude, the better the OHC function [25, 26].

OBJECTIVE

The aim of the presented interdisciplinary study was to assess whether some modifiable factors, such as HbA_{1c} level, blood pressure, serum lipids and BMI have an impact on auditory organ function measured by pure-tone audiometry

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and transient-evoked otoacoustic emissions (TEOAE) among the relatively young type 1 and type 2 diabetic subjects with a short duration of the disease.

MATERIALS AND METHOD

Participants. 58 patients were included, 31 with type 1 diabetes and 27 with type 2 diabetes, without any history of occupational noise exposure and/or ototoxic medication use, and without clinically overt hearing impairment or diabetic neuropathy. All subjects were below 45 years of age, to avoid the impact of presbycusis, and had diabetes duration of less than 10 years, to avoid the impact of diabetic microvascular complications. Among the study participants, 5 subjects had early background retinopathy, 4 had microalbuminuria, 26 patients received anti-hypertensive drugs, 17 subjects were overweight and 14 were obese (Tab. 1).

Table 1. Characteristics of the study group; numerical data presented as mean \pm SD.

Parameter	All participants	Type 1 diabetes	Type 2 diabetes	p value (type 1 vs. type 2 diabetes)
Age (years)	33.7 \pm 7.9	29.1 \pm 7.1	39.0 \pm 4.6	<0.001
Diabetes duration (years)	4.1 \pm 2.8	4.6 \pm 2.7	3.5 \pm 2.9	N.S.
HbA _{1c} (%)	7.16 \pm 1.57	7.67 \pm 1.47	6.56 \pm 1.46	0.011
Blood lipids				
Total cholesterol (mg/dl)	182.0 \pm 35.8	178.9 \pm 41.1	186.2 \pm 26.8	N.S.
HDL cholesterol (mg/dl)	52.6 \pm 14.6	57.8 \pm 14.6	46.2 \pm 11.8	0.003
LDL cholesterol (mg/dl)	107.2 \pm 32.8	101.7 \pm 38.7	114.0 \pm 21.5	N.S.
Triglycerides (mg/dl)	108.0 \pm 69.6	90.4 \pm 68.8	130.0 \pm 64.0	0.007
Eye fundus				
Normal (n)	49	27	22	N.S.
Background retinopathy (n)	5	3	2	N.S.
Not performed (n)	4	1	3	
Albumin excretion (mg/l)				
Normal (n)	47	29	18	N.S.
Microalbuminuria (n)	4	1	3	N.S.
Not performed (n)	7	1	6	
Hypertension (n)				
Systolic blood pressure (mm Hg)	137.4 \pm 18.0	131.6 \pm 13.1	144.0 \pm 20.3	0.021
Diastolic blood pressure (mm Hg)	81.3 \pm 12.1	75.7 \pm 7.3	87.7 \pm 13.3	<0.001
BMI (kg/m ²)				
Normal (n)	27	24	3	<0.001
Overweight (n)	17	6	11	(for
Obese (n)	14	1	13	trend)
Hearing				
Normal (n)	38	23	15	N.S.
Impaired (n)	20	8	12	N.S.
TEOAE amplitude (dB)	7.44 \pm 4.02	7.75 \pm 4.43	7.09 \pm 3.80	N.S.
TEOAE present (n)	42	24	18	N.S.
Lack of TEOAE (n)	16	7	9	N.S.

N.S. – non significant

After informed consent was obtained, vital signs were measured, and urine and blood samples were taken for laboratory evaluations. Then patients were referred to the audiological laboratory in the Department of

Otorhinolaryngology at the Voivodeship Specialistic Hospital in Rzeszów, Poland. After a detailed ENT examination by the same ENT specialist (to exclude external and middle ear abnormalities), pure-tone audiometry and otoacoustic emissions were evaluated.

Pure-tone audiometry was performed in a sound-proof booth, using a Madsen OB822 audiometer (GN Otometrics, Taastrup, Denmark) with Telephonics TDH 39 earphones. Air conduction was measured at a frequency range of 125–12,000 Hz, and bone conduction measured at frequencies 250–6,000 Hz. The initial stimulus was 10 dB. The level was then increased by 5-dB steps. Mild hearing impairment was recognized at a hearing threshold above 20 dB, and moderate impairment above 40 dB in at least one frequency [27].

Transient evoked otoacoustic emissions (TEOAE), were evaluated using a Scout Sport 580-OAE SP6 Analyzer (Biologic System Corp., Mundelein, IL, USA) with a 'non-linear' click stimulus of 80 μ s duration, repetition rate of 50 Hz, and intensity equal to \sim 80 dB. The results were presented in dB as a mean of signal to noise ratio for a band range of 1.2–3.5 kHz, and also for particular frequencies of the TEOAE spectrum: 1, 1.5, 2, 3 and 4 kHz. The mean TEOAE amplitude below 6 dB in a band range 1.2–3.5 kHz was considered as a lack of otoacoustic emission [26].

Body weight and height were measured using legalized electronic medical scales WPT 150.0 (Radwag, Radom, Poland), after which the BMI was calculated.

Blood pressure was measured after at least 5 minutes of rest, in the sitting position, using an automatic Omron 705 IT blood pressure monitor (Omron Healthcare Europe BV, Hoofddorp, The Netherlands).

Lipid parameters were measured using an Architect c8000 analyser (Abbott Laboratories, Irving, TX, USA) in the 'Medicor' Medical Diagnostic Centre in Rzeszów, Poland.

The metabolic control of diabetes was determined by HbA_{1c} measurement, and presence of microalbuminuria determined by the albumin concentration and albumin/creatinine ratio assessment from a morning sample of urine. Both measurements were performed using a DCA 2000+ analyzer (Siemens, Elkhart, IN, USA) with the monoclonal antibody method.

To assess the presence of retinopathy eye fundus examination by an ophthalmologist was performed.

Statistical analysis. Statistical analysis of the data was performed using SigmaPlot for Windows version 12.3 (Systat Software Inc., San Jose, CA, USA). The numerical data comparing two groups of patients were analyzed using an unpaired Student's t-test, after performing a Shapiro-Wilk normality test and constant variance test. In the case of normality and/or constant variance test failure, the Mann-Whitney rank sum test was performed. The categorical data were compared using χ^2 test. The linear correlations between the hearing function and HbA_{1c}, blood pressure values, lipid parameters or BMI were analyzed using the Spearman rank order correlation test. To assess the impact of other variables, multiple linear regression or multiple logistic regression tests were performed. Numerical data are expressed as mean \pm SD. A p value <0.05 was considered statistically significant.

RESULTS

Separate analyses were performed for patients with type 1 and type 2 diabetes; however, due to the small sample size in each group, only a few significant differences were found between patients with normal and impaired hearing, as well as between subjects with TEOAE present and absent.

Among people with type 1 diabetes, subjects with normal hearing had borderline significantly lower BMI (22.2 kg/m² vs. 25.0 kg/m², $p=0.050$) in relation to patients with impaired hearing. Also a non-significant trend toward higher HDL cholesterol was found in this group (60.8 mg/dl vs. 49.5 mg/dl, $p=0.061$). Among people with type 2 diabetes, hearing subjects with normal hearing had significantly higher HDL cholesterol (51.8 mg/dl vs. 40.6 mg/dl, $p=0.018$), compared with patients with impaired hearing. In the linear correlations analyses among type 1 diabetic subjects, a weak significant association between hearing impairment and BMI (coefficient $R=0.363$, $p=0.045$) was revealed. Also, a positive linear correlation between triglycerides and hearing threshold at 1,000 and 2,000 Hz, as well as between BMI and hearing threshold at 4,000, 8,000 and 12,000. Among patients with type 2 diabetes, the only significant relationship was a weak negative correlation between hearing impairment and HDL cholesterol level ($R=0.410$, $p=0.046$).

Both among type 1 and among type 2 diabetes patients no significant differences between subjects with TEOAE present and absent were found. Only a trend towards higher BMI among type 1 diabetes and lower HDL cholesterol among type 2 diabetes among patients with absent TEOAE was revealed. In the linear correlations analyses, the only finding was a positive relationship between HDL cholesterol and TEOAE amplitude ($R=0.441$, $p=0.031$).

Taking into consideration that type 1 and type 2 diabetic patients appeared to share similar risk factors for auditory organ impairment and, despite notable differences between several variables in each group, statistical significance was weak or was lacking, it was decided to combine these two groups to increase the statistical power of the findings.

In the combined group, 38 patients had normal hearing; hearing impairment was found in 20 subjects (34.5%), 8 with type 1 and 12 with type 2 diabetes. These patients had a significantly lower HDL-cholesterol concentration and a higher BMI. A trend towards a higher triglycerides level was also observed (Tab. 2 and Fig. 1). After adjustment for age, only

Table 2. Values of different variables among patients with normal hearing and hearing impairment (mean \pm SD).

Variable	Normal hearing (n=38)	Hearing impairment (n=20)	p value	p value adjusted to age
Age (years)	31.9 \pm 7.6	37.3 \pm 7.3	0.012	-
HbA _{1c} (%)	7.37 \pm 1.72	6.79 \pm 1.20	0.184	-
HDL-cholesterol (mg/dl)	57.6 \pm 13.1	44.2 \pm 13.4	<0.001	0.007
LDL-cholesterol (mg/dl)	107.6 \pm 33.3	106.5 \pm 32.7	0.903	-
Triglycerides (mg/dl)	93.6 \pm 59.8	132.4 \pm 79.5	0.059	-
Systolic blood pressure (mm Hg)	135.4 \pm 18.5	141.1 \pm 16.8	0.262	-
Diastolic blood pressure (mm Hg)	79.9 \pm 13.1	83.8 \pm 9.8	0.067	-
BMI (kg/m ²)	25.5 \pm 6.4	29.6 \pm 6.3	0.023	0.154

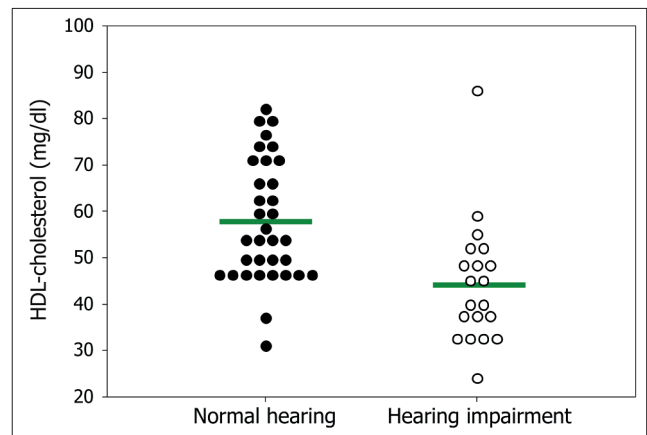


Figure 1. HDL-cholesterol among patients with normal hearing and hearing impairment (histogram plot and mean).

the HDL-cholesterol level appeared to be significantly lower among patients with hearing impairment. No significant differences were found between the two groups regarding HbA_{1c}, blood pressure and LDL-cholesterol.

In the univariate linear correlation analysis, a significant negative relationship between hearing threshold and HDL-cholesterol (at frequencies from 1,000 Hz to 12,000 Hz), as well as positive correlation between hearing threshold and triglycerides (at frequencies from 1,000 Hz – 4,000 Hz), BMI (at frequencies from 2,000 Hz – 12,000 Hz) and systolic blood pressure (SBP) (at frequencies 2,000 Hz and 3,000 Hz) were found. After adjustment for age, only triglycerides at the frequency of 1,000 Hz and HDL-cholesterol at frequencies 3,000, 4,000, 8,000 and 12,000 Hz remained to significantly correlate with hearing threshold at these frequencies.

Normal TEOAE amplitude was found among 42 patients. Absence of otoacoustic emissions was diagnosed in 16 subjects (27.6%), 7 with type 1 and 9 with type 2 diabetes. In this group, a significantly lower HDL-cholesterol level was found (Tab. 3, Fig. 2). No significant differences regarding other variables were demonstrated between the two groups.

In the univariate linear correlation analysis, a significant positive relationship between TEOAE amplitude and HDL-cholesterol ($R=0.333$, $p=0.014$), and a negative correlation between TEOAE amplitude and triglycerides ($R=-0.277$, $p=0.043$) were demonstrated. However, after adjustment for age, these relationships did not remain significant.

The likelihood of hearing impairment was significantly lower among patients with a higher HDL-cholesterol

Table 3. Values of different variables among patients with otoacoustic emissions present and absent.

Variable	TEOAE present (n=42)	TEOAE absent (n=16)	p value
Age (years)	32.5 \pm 8.0	36.9 \pm 6.7	0.051
HbA _{1c} (%)	7.23 \pm 1.60	6.97 \pm 1.53	0.751
HDL-cholesterol (mg/dl)	55.2 \pm 13.1	45.4 \pm 13.4	0.018
LDL-cholesterol (mg/dl)	106.7 \pm 33.1	108.4 \pm 32.9	0.869
Triglycerides (mg/dl)	101.9 \pm 63.4	125.3 \pm 85.4	0.471
Systolic blood pressure (mm Hg)	136.1 \pm 17.9	140.6 \pm 18.2	0.400
Diastolic blood pressure (mm Hg)	80.6 \pm 10.8	83.1 \pm 15.2	0.676
BMI (kg/m ²)	26.2 \pm 6.9	28.8 \pm 5.6	0.077

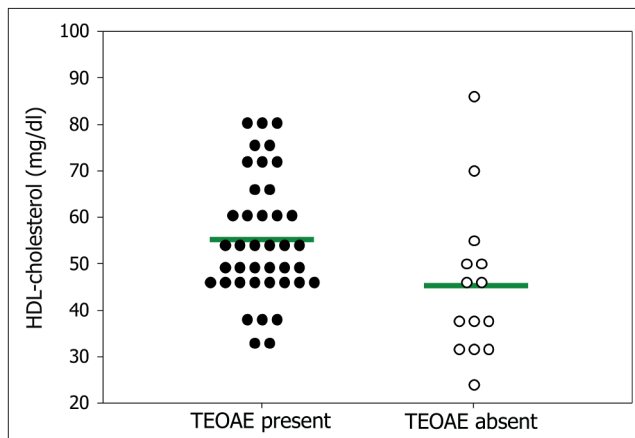


Figure 2. HDL cholesterol among patients with otoacoustic emissions present and absent (histogram plot and mean).

concentration (≥ 50 mg/dl), compared with subjects with a lower HDL-cholesterol level: odds ratio (OR) 0.182 ($p=0.011$), even after adjustment for age (adjusted OR 0.242, $p=0.035$). Patients with HDL-cholesterol level ≥ 50 mg/dl also had a significantly lower hearing threshold at frequencies from 500 Hz – 12,000 Hz (Fig. 3A), as well as higher TEOAE amplitude (Fig. 4).

Subjects with triglycerides level above median (89 mg/dl) had a significantly higher hearing threshold at frequencies from 500 Hz – 12,000 Hz (Fig. 3B), as well as lower TEOAE amplitude (Fig. 4).

Patients with elevated BMI (≥ 25 kg/m²) had a significantly higher hearing threshold at frequencies from 2,000 Hz – 12,000 Hz (Fig. 3C), as well as lower TEOAE amplitude (Fig. 4).

No significant differences were revealed between groups of patients with HbA_{1c} level >7.0 % vs. ≤ 7.0 %, with LDL-cholesterol concentration ≥ 100 mg/dl vs. <100 mg/dl, with SBP value ≥ 130 mm Hg vs. <130 mm Hg, and with DBP ≥ 80 mm Hg vs. <80 mm Hg, with regards to hearing threshold at particular frequencies and TEOAE amplitude.

DISCUSSION

The presented study demonstrates that, apart from known risk factors responsible for hearing loss, several other factors may influence the hearing function among diabetic patients. HDL cholesterol concentration, triglycerides level, and BMI appear to be associated with the auditory organ function in the diabetic population.

The association between HbA_{1c} and hearing function has been discussed in several papers. In some studies, correlation between poor metabolic control and higher hearing thresholds was found [8,19]; other studies, however, have not confirmed such a relationship [9, 11, 13, 15, 20]. In one study, type 1 diabetic patients with HbA_{1c} level $<7.0\%$ demonstrated higher TEOAE amplitude in comparison with subjects with lesser metabolic control [9]. However, this was not observed in other studies [11, 13]. In the presented study, HbA_{1c} level appeared not to be associated either with hearing threshold, or with TEOAE amplitude.

The correlation between hypertension and hearing loss in the non-diabetic population has also been documented in several studies. The relationship between hypertension

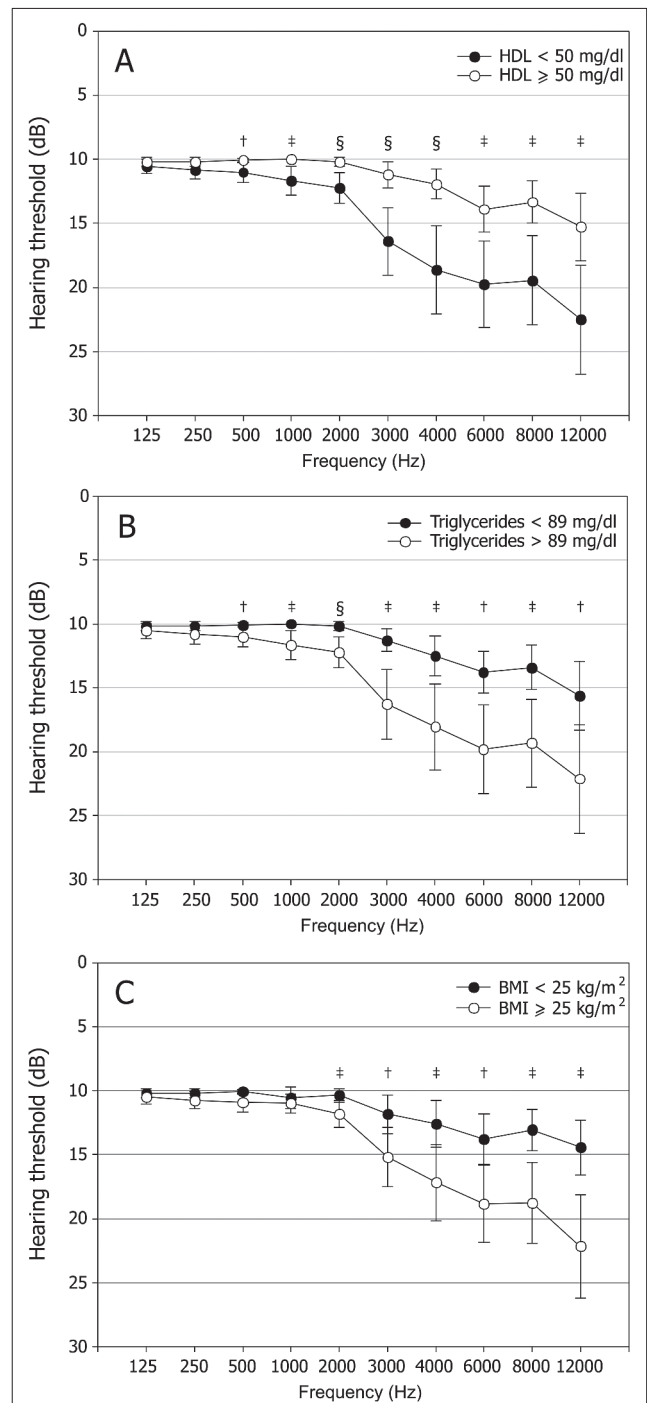


Figure 3. Audiometric curves in relation to HDL cholesterol (A), triglycerides (B), and BMI (C) (mean \pm SD); † $p<0.05$. ‡ $p<0.01$. § $p<0.001$

and hearing impairment was demonstrated in a middle-age population by de Moraes Marchiori et al. Patients with hypertension had doubled risk of hearing loss relative to normotensive subjects, OR 2.06 (95% CI 1.26–3.39), $P=0.0034$ [28]. Amongst iron and steel industry workers in India who were exposed to noise, hypertension was more prevalent among those who had hearing impairment than among those who had normal hearing [29]. In the study by Esparza et al., patients with hypertension had a higher hearing threshold at 8 kHz and had more prevalent abnormal otoacoustic emissions than normotensive subjects. These findings correlated with the degree of retinal vascular

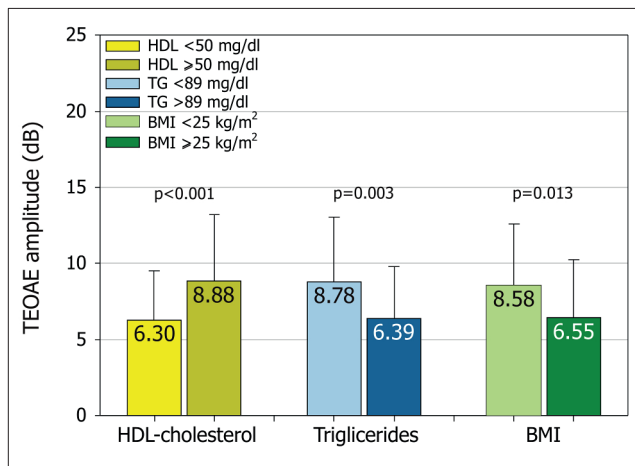


Figure 4. Otoacoustic emissions amplitude with regards to HDL cholesterol, triglycerides and BMI (mean \pm SD).

compromise among hypertensive patients [30]. However, a relationship between hearing function and hypertension was not found not in every study. Torre III et al. did not reveal any correlation between hypertension and hearing impairment, neither in pure-tone audiometry nor in distortion product otoacoustic emissions (DPOAE) in older adults [31].

Jørgensen and Buch, in a diabetic population did not find any relationship between blood pressure value and hearing thresholds in the pure-tone audiometry [22]. On the contrary, Duck et al. revealed an association between hypertension and hearing thresholds at high frequencies (4 – 8 kHz) [21]. In the presented study, neither systolic nor diastolic blood pressure values appeared to have a significant impact on hearing thresholds or the TEOAE amplitude.

The association between hyperlipidaemia and hearing loss has been evaluated in several studies. Triglycerides appeared to have a negative impact on hearing thresholds [32, 33], as well as on otoacoustic emissions [23, 32]. This was not supported in only one, older paper [34]. In the presented study, patients with a higher triglycerides level had a significantly higher hearing threshold in pure-tone audiometry at the low, middle and high frequencies, and also a lower amplitude of otoacoustic emissions.

Data regarding hypercholesterolaemia and the hearing function are divergent. In three out of the four of the above-mentioned earlier studies neither LDL nor HDL cholesterol concentration show an association with the hearing function [23, 32, 33]. However, such a relationship was revealed in a study by Preyer et al. Patients with a more profound DPOAE (distortion product otoacoustic emissions) abnormalities appeared to have higher LDL cholesterol levels [35]. The impact of an elevated cholesterol concentration on hearing is also supported by an experimental study carried out by Satar et al. [36]. They revealed that guinea pigs exposed to a very high cholesterol diet, developed profound oedema in the stria vascularis, and also mild oedema of the OHC. These changes were predominantly seen in the basal turn of the cochlea. However, in the presented study, LDL cholesterol level did not appear to have any impact on either hearing threshold or on TEOAE amplitude.

In the studies by Evans et al., and Chang et al., the HDL cholesterol level appeared to have no impact on audiological test results [32, 33]. However, in the study by Suzuki et al., low HDL cholesterol concentration showed a relationship

with a higher hearing thresholds at 2,000 Hz and 4,000 Hz [34]. Also, in our observation, HDL cholesterol level was inversely correlated with hearing thresholds throughout almost the whole frequency range. In the diabetic population drawn from the National Health and Nutrition Examination Survey (NHANES), neither the total cholesterol level nor hypertension appear to be correlated with hearing impairment assessed by pure-tone audiometry. However, hearing impairment was significantly more prevalent among patients with a low HDL cholesterol level across the whole frequency range [20, 37]. This supports the hypothesis of a potentially protective role of HDL cholesterol on the hearing function in the diabetic population. In the above-mentioned papers, a relationship between hearing threshold and triglycerides was not studied.

In a large population-based study, body mass index appeared to correlate with a higher hearing threshold across the whole frequency range [2]. Also, in the study by Bainbridge et al., BMI was associated with hearing impairment, but only at high frequencies (3,000 Hz – 8,000 Hz) [37]. In the presented study, a relationship between BMI and hearing thresholds was also discovered, which was similar to a study by Bainbridge et al. in which hearing was affected at middle and high frequencies (2,000 Hz – 12,000 Hz). Additionally, we revealed a correlation between BMI and otoacoustic emissions – overweight and obese subjects had significantly lower TEOAE amplitude. This finding needs to be confirmed on a larger group of patients, because this has not yet been studied.

Amongst limitations of the presented study, the most important seem to be the relatively small number of participants. Due to this fact, despite statistical significance, the random effect of some findings cannot be totally excluded. The other limitation is the non-homogeneous group of patients which included patients with both type 1 and type 2 diabetes. Although no significant differences in the prevalence of hearing impairment and TEOAE abnormalities between these two groups were found, patients with type 2 diabetes were older, more obese, had better metabolic control, higher SBP and DBP, and worse lipid profile in comparison with type 1 diabetic subjects.

CONCLUSIONS

The presented study demonstrated that several modifiable risk factors, such as HDL cholesterol concentration, triglycerides level and body mass index may have an impact on hearing function among diabetic subjects. The differences in characteristics of type 1 and type 2 diabetic patients may indicate that different mechanisms could be involved in abnormal hearing function among these two types of diabetes. However, lipid abnormalities, frequently associated with increasing BMI, seem to play an important role in the development of hearing disturbances in both type 1 and type 2 diabetes. To determine the role of other variables, studies on a larger sample of patients are required.

If the presented findings are confirmed, a vast area of possible interventions for the preservation of the hearing function in this population will be opened. Various hypolipaeamic drugs, as well as weight-reducing interventions may be useful, but further prospective, interventional studies are required to determine the value of such treatment methods.

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