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Evaluation of Hearing in Children with Metabolic Syndrome

Original Investigation
Özgün Araştırma

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Abstract

Objective: The frequency of metabolic syndrome is increasing in both children and adults. In addition to metabolic complications such as obesity, hypertension, cardiovascular diseases, insulin resistance, and type 2 diabetes, metabolic syndrome may affect all systems of the body. The aim of the present study was to investigate the effect of metabolic syndrome on hearing in childhood.

Methods: A prospective, controlled study was performed on 38 obese children diagnosed with metabolic syndrome and 34 healthy children. Anthropometric measurements and biochemical studies were performed. All individuals underwent pure-tone audiometry, tympanogram, and transient evoked otoacoustic emission (TEOAE) tests. The hearing thresholds of the patients were compared with healthy volunteers.

Results: There was no significant difference in terms of age and gender between the groups (p>0.05). There was no significant difference in mean hearing levels between the groups. When frequencies were compared, significantly increased hearing threshold levels were determined at low frequencies in children with metabolic syndrome. Analysis of the TEOAE results elicited no statistically significant variation in terms of signal-to-noise ratio values, signal amplitudes, or test reproducibility values between the study groups.

Conclusion: Identification of the potential hearing losses early by means of detailed hearing examinations in children with metabolic syndrome is important. To the best of our knowledge, this is the first study to examine the effect of metabolic syndrome on hearing in this age group.

Keywords: Childhood, metabolic syndrome, hearing, audiometry

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Introduction

The International Diabetes Federation (IDF) has defined metabolic syndrome as the presence of two of the following findings in addition to obesity: increased triglyceride (TG), low high-density lipoprotein (HDL) cholesterol, high blood pressure, or high plasma glucose levels (1, 2). Currently, up to one-quarter of the adult population is reported to have metabolic syndrome, and the prevalence of the disease is increasing rapidly among children and adolescents due to the rise in obesity among young people. Obesity is recognized as a "sine qua non" for metabolic syndrome. It has currently become a major health problem in children, as well as in adults. The World Health Organization reported that 41 million children below the age of 5 years in 2014 are overweight or obese, and that the number has doubled since 1990 (3). In addition, the harmful effects of obesity on health beginning in childhood are reported to be greater than those beginning in adulthood (4).

Metabolic syndrome arising in childhood can lead to problems affecting several systems, including respiratory problems, musculoskeletal system diseases, and a predisposition to some forms of cancer, in addition to cardiovascular complications and diabetes. In hearing, the most important receptors in the inner ear are the hair cells in the cochlea. Mature cochlear hair cells in mammals cannot be regenerated, and losses result in permanent hearing impairment. Cochlear injury equates to damage to all or part of the inner ear and causes sensorineural hearing loss.

To the best of our knowledge, this is the first study to specifically examine auditory functions in children with metabolic syndrome compared with control subjects with no metabolic syndrome. Hearing loss emerging in association with various etiological factors in children is too common to be ignored. Mild hearing loss may be undetected by both families and physicians performing routine examinations (5, 6). The aim of the present study was to investigate whether hearing loss develops in children with metabolic syndrome.

Methods

This prospective, controlled study included patients under outpatient observation due to metabolic syndrome at the Pediatric Endocrinology Department and healthy children. The local ethical committee of Atatürk University School of Medicine approved the study (admission no. 2017:1-2). Parental consent was obtained for children to be enrolled in the present study.

All children included in the study were weighed and measured. Measurements were performed by the same individual, with children removing their shoes and outer clothing, using the same scales and measures. An ideal body weight and body mass index were calculated for each child using the height and weight values obtained. The ideal body weight was obtained by dividing the actual weight by ideal weight and multiplying by 100. Children were classified by weight by comparing ideal weight values obtained for each child with age-adjusted international cut-off values.

Participants within 90%-110% of the ideal body weight percentage were enrolled in the control group (CG), whereas those above 120% were included in the obese group. Subjects with an ideal body weight percentage of 110%-120% were excluded from the study.

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Subjects with a BMI for height and weight in the 85-95th percentiles were classified as overweight, and those above the 95th percentile as obese.

Blood pressure was measured using a standard cuffed manometer. Two measurements were performed at a 10-minute rest period interval with an age-appropriate cuff covering two-thirds of the left upper arm. The mean value was recorded. Subjects with systolic or diastolic blood pressure above the 95th percentile for sex and age were classified as hypertensive.

Venous blood specimens were collected from all children following a 12-hour overnight fasting for glucose, insulin, cholesterol, and TG level measurements. An oral glucose test was administered to all children.

Biochemical analysis

Venous blood specimens collected following a 12-hour overnight fasting were placed in straight tubes and centrifuged at 4000 rpm for serum separation. Then, specimens were stored at –80°C until use to investigate biochemical parameters. Specimens were removed on the day of the study and left to thaw at a room temperature of 22°C.

Total TG, HDL, and glucose were studied using a Roche kit and an auto analyzer. Insulin was measured by a chemiluminescence method using a BIO-DPC kit and an IMMULITE 2000 device (Siemens, Germany).

A fasting blood glucose level ≥100 mg/dL was considered as impaired fasting glucose, and a level ≥126 mg/dL was defined as diabetes. In the oral glucose tolerance test, a dose of 1.75 g glucose/kg was used until a maximum of 75 g. Venous plasma glucose and insulin levels were collected at 0, 30, 60, and 120 minutes. A second-hour blood glucose <140 mg/dL was defined as normal, 140–200 mg/dL as impaired glucose tolerance, and ≥200 mg/dL as diabetes. Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR; fasting insulin pmol/L × fasting glucose mmol/L/22.5) method. The presence of insulin resistance was defined as HOMA-IR >3.16 (7). A fasting HDL level ≤40 mg/dL and a fasting TG level ≥110 mg/dL were defined as dyslipidemia. Diagnosis of metabolic disease was based on the criteria set out by the IDF (1).

Hearing evaluation

Otolaryngological examination was performed by an experienced otolaryngologist. All examinations were carried out by the same otolaryngologist, after which tympanogram, pure-tone audiometry (PTA), and transient evoked otoacoustic emission (TEOAE) tests were conducted. Children below 8 years were excluded from the study owing to their inability to perform PTA.

Tympanometry

Tympanometry and acoustic reflex tests were performed on all subjects using Interacoustics AT 235h tympanometer (Interacoustics, Middelfart, Denmark).

Pure-tone audiometry

All children underwent PTA using a Maico MA 53 device (Maico Diagnostics, Berlin, Germany). The test was performed in a commercially available double-walled, sound-treated room by an experienced audiologist. Sound at different frequencies and loudness levels was administered directly to the patients' ears. Then, they were told to respond by raising their hands or pushing the button when they heard the sound tone. The minimum level of response was adopted as the threshold level for each frequency. Air conduction thresholds were recorded at 250, 500, 1000, 2000, 4000, and 8000 Hz, and bone thresholds were recorded at 500, 1000, 2000, and 4000 Hz frequencies. The mean hearing thresholds across frequency and for individual frequencies were compared with those of the control subjects.

Transient evoked otoacoustic emissions

All subjects' TEOAE tests were conducted by an experienced audiologist inside a specially sound-proofed room using a Vivosonic Integrity Evoked Potentials System device (Vivosonic Inc., Toronto, Canada). The click stimulus method was employed. The signal-to-noise ratio (SNR) was determined at four separate frequencies (1, 2, 3, and 4 kHz). The SNR findings from the study group and CG were measured for each frequency and then compared. The SNR defines the difference between emission amplitude and noise floor. Signal amplitude and test reproducibility findings were also recorded for all participants.

On physical examination, patients with acute or chronic otitis media, tympanic membrane perforation, a previous history of otological surgery, non-type A results at tympanogram, a fail report at acoustic reflex test, or air-bone gap observed at audiometry were excluded from the study. Subjects with syndromic obesity (e.g., Alström syndrome and Bardet–Biedl syndrome) were also excluded.

Power analysis

The preliminary outcome of the study was the difference in hearing thresholds. In our preliminary study, the main difference was observed at 250 and 500 Hz frequencies. The standard deviation (SD) of hearing thresholds at 250 Hz was determined at 5.3 in the study group and 5.0 in the CG. The expected difference in the hearing threshold was at least 5 dB. Therefore, with 38 patients in the study group and 34 individuals in the CG, the power of the study was calculated as 98%, with an alpha error of 0.05 using a Russ Lenth Piface Java module.

Statistical analysis

Statistical analysis was performed by SPSS for Windows 17.0 software (SPSS Inc., Chicago, IL, USA). Data were expressed as mean±SD. The Mann–Whitney U test was used to compare the quantitative values. A p-value <0.05 was accepted as statistically significant.

Results

The study group consisted of 38 patients (18 males and 20 females) aged 8-18 years who were diagnosed with metabolic syndrome. The CG included 34 healthy volunteers (16 males and 18 females) aged 10-17 years. The mean ages of the study group and CG were 13.1±2.5 years and 13.0±2.8 years, respectively. There was no statistically significant difference in terms of age between the groups (p=0.72). Table 1 summarizes the anthropometric measurements and blood pressure values of the groups. Table 2 shows the biochemical analysis.

For all frequencies, the mean hearing thresholds were 12.6 dB in the right ears and 11.9 dB in the left ears in the study group and 13 dB in the right ears and 12.2 dB in the left ears in the CG. There was no significant difference in mean hearing levels between the groups. When frequencies were compared individually, the hearing thresholds of the patient group at 250 and 500 Hz were significantly higher than those of the control subjects in the left ears, and the hearing thresholds at 250, 500, and 1000 Hz were higher in the right ears (Figure 1, 2).

Analysis of the TEOAE results elicited no statistically significant variations between the two groups' SNR values or signal amplitudes. In addition, there was no statistically significant difference in terms of test reproducibility values between the study group (62±9.6 in the right ear and 59.4±12.2 in the left ear) and the CG (64.1±8.4 in the right ear and 61.4±7.2 in the left ear) (p>0.05). Table 3 shows the TEOAE test parameters.

Table 1. Anthropometric measurements and blood pressure values of the groups

	Study group n=38	Control group n = 34	p
Height (cm)	149.3±17.4	148.7±16.8	p>0.05
Weight (kg)	62.1±19.4	42.5±13.6	p<0.001*
BMI (kg/m^2)	28.1±3.4	18.6±2.2	p<0.001*
Relative weight (%)	143.2±18.5	101±6.8	p<0.001*
Systolic blood pressure (mm Hg)	118.0±17.9	99.8±13.2	p<0.05*
Diastolic blood pressure (mm Hg)	71.0±8.3	69.2±7.9	p>0.05

*Statistically significant
BMI: body mass index

Table 2. Biochemical analysis of the study and control groups

	Study group n=38	Control group n=34	p
Fasting blood glucose level	106±5.3	79.2±8.1	<0.001*
Fasting insulin	18.5±5.6	10.3±5.2	<0.05*
HOMA-IR	3.9±2.5	2.1±2.1	<0.05*
HbA1c	5.9±0.3	5.1±0.2	<0.001*
Triglyceride	152.3±76.4	98.2±42.7	<0.001*
Total cholesterol	168.6±32.9	108.1±29.7	<0.001*
HDL	38.8±6.4	45.8±7.8	<0.05*
LDL	11.8±22.3	76±24.5	<0.001*
AST	38.2±10.1	29.4±9.1	>0.05
ALT	32.7±5.6	26.1±4.5	>0.05

*Statistically significant
HOMA-IR: homeostasis model assessment of insulin resistance; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein; AST: aspartate aminotransferase; ALT: alanine aminotransferase

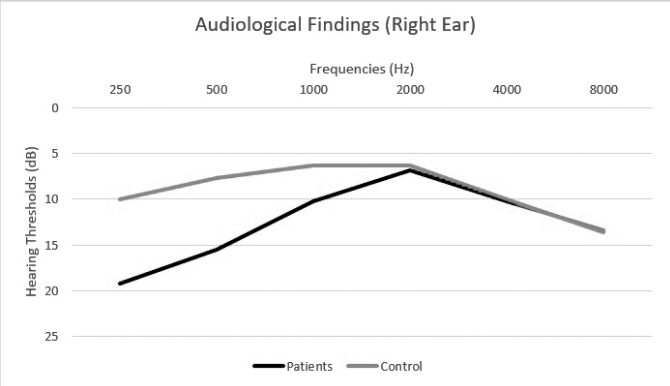

Figure 1. Audiological findings of patients and control group (right ear)

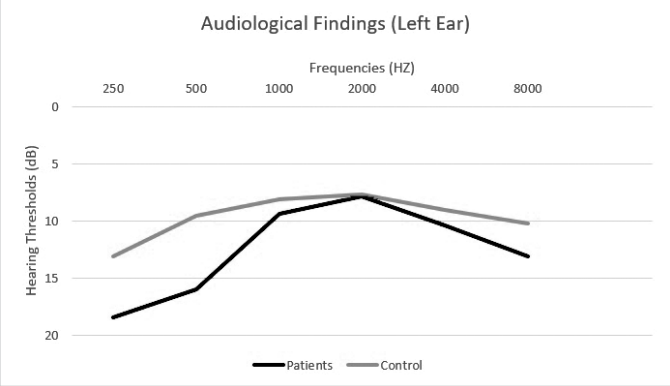

Figure 2. Audiological findings of patients and control group (left ear)

Table 3. SNR levels for each frequency

	Right ear			Left ear		
Frequency (Hz)	**Patients**	**Control**	**p**	**Patients**	**Control**	**p**
1000	8.3±3.4	8.6±4.2	>0.05	8.7±2.8	9.1±3.4	>0.05
2000	7.5±4.8	8.1±3.2	>0.05	7.4±3.5	8.2±3.3	>0.05
3000	7.3±3.1	7.6±3.5	>0.05	5.8±2.1	6.2±3.4	>0.05
4000	6.8±2.4	7.1±3.9	>0.05	5.7±3.1	6±3.6	>0.05
Reproducibility	62±9.6	64.1±8.4	>0.05	59.4±12.2	61.4±7.2	>0.05

SNR: signal-to-noise ratio

Discussion

Metabolic syndrome is a disease that affects numerous systems in the body, with the most significant finding being obesity. Excessive weight gain beginning in childhood sets the framework for adult obesity. Overweight in childhood is a powerful marker of overweight at later ages (4, 7). Obesity can cause significant complications both physical and psychological. Complications arise earlier and more frequently as the duration and severity of obesity increase. This also increases the significance of childhood obesity. This disease affects the psychosocial state, as well as the endocrine system, gastrointestinal system, skin, genitourinary system, and musculoskeletal system, in varying degrees. It is known that obesity in childhood and adolescence leads to diabetes mellitus, hypertension, stroke, dyslipidemia, cardiovascular diseases, gall bladder diseases, respiratory system problems, cancer, arthritis, and gout in adulthood. The risk factors for obesity should be investigated, and early diagnosis should be made to prevent obesity-related complications (8, 9).

Results of previous studies investigating the relationship between obesity and hearing loss are controversial. Some studies have reported no association between obesity and hearing loss. However, there is still inconsistency in studies reporting that obesity leads to hearing loss regarding the frequency range affected. In their study of men aged 40-74 years, Shargorodsky et al. (10) concluded that obesity is not a risk factor for hearing loss. Hwang et al. (11) reported that obesity is associated with hearing loss involving high frequencies in women aged over 55 years and with hearing loss at both high and low frequencies in men below 55 years. Their study also determined no correlation between hearing and obesity in men aged over 55 years or women below 55 years (11). Kim et al. (12) suggested that an increased visceral adipose tissue in adult obese women increases hearing thresholds, but observed no such relationship in men. In addition, they observed that a decrease in adipose tissue improves hearing thresholds. Ucler et al. (13) showed that high-frequency hearing thresholds in adult obese women are significantly higher than those in the CG. Lalwani et al. (14) also determined that low-frequency thresholds in obese adolescents are significantly higher than those in the CG. However, they noted no significant difference between the two groups in terms of high-frequency ranges. In a study of 4083 patients, Fransen et al. (15) reported that high body weight impairs hearing thresholds at low frequencies, but that high BMI values are associated with both low- and high-frequency hearing losses. In our study, we also determined that low-frequency hearing thresholds in children with metabolic syndrome were significantly higher than those in the CG.

The other components of metabolic syndrome, in addition to obesity, are impaired glycemic control, hypertension, and dyslipidemia. Many studies have also revealed the effects of these conditions on hearing. In their study of type 2 diabetes and hearing, Zivkovic-Marinkov et al. (16) reported significantly impaired hearing in patients with type 2 diabetes compared with the CG and also suggested that prolongation of uncontrolled glycemia exacerbates hearing loss. Bener et al. (17) found greater compromise of hearing in patients with diabetes with accompanying hypertension and also observed more widespread complications such as nephropathy, neuropathy, and retinopathy in patients with diabetes with poor hearing. Shargorodsky et al. (10) reported that hypercholesterolemia increases the risk of hearing loss in adult men. Evans et al. (18) also noted that chronic dyslipidemia with accompanying high TG levels can lead to a decrease in hearing functions.

Although the relationship between metabolic syndrome and hearing loss has not been fully elucidated, the underlying mechanism is thought to be multifactorial. Metabolic syndrome can

cause hearing loss either directly or indirectly. Imbalances in the oxidant–antioxidant system, micro- and macroangiopathies and neuropathies may represent factors directly affecting the cochlear system (19). Additionally, the components of metabolic syndrome such as diabetes, dyslipidemia, and hypertension can affect the hearing system indirectly. Indeed, an increased risk of low-frequency hearing loss has been reported in subjects with cardiovascular disease, and this has been attributed to strial dysfunction deriving from vascular disease (14). Moreover, Satar et al. (20) showed that dyslipidemia can cause cochlear injury, leading to edema in the outer hair cells and the strial vascular layer. Aladag et al. (21) reported that oxidative stress plays a major role in the development of hearing loss in patients with diabetes. The existing hypotheses in all these studies do not fully explain the pathophysiology of hearing loss. Since the aim of our study was to examine whether metabolic syndrome causes hearing loss, the effect of metabolic syndrome on hearing loss was not investigated.

The present study has a number of limitations. First, no investigation was performed on proinflammatory cytokines and oxidant–antioxidant substance levels that affect hearing. Second, the patient population was small. Third, the present study represented cross-sectional research in which patients were not followed up long term. Further research is needed in the future to evaluate the effect of metabolic syndrome and associated comorbidities on hearing and to determine the pathophysiological changes involved.

Conclusion

Metabolic syndrome can affect several systems in the body and can have an adverse impact on the hearing system in children. We determined significantly higher hearing thresholds at low frequencies in children with metabolic syndrome compared with the controls. These changes in hearing can be overlooked by families and physicians in childhood and can have adverse impacts on children's social development, academic success, and cognitive functions. It is therefore important for potential hearing losses to be identified early by means of detailed hearing examinations in children with metabolic syndrome.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Atatürk University School of Medicine (2017:1-2).

Informed Consent: Written informed consent was obtained from the parents of the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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