ORIGINAL ARTICLE

Cochleovestibular Dysfunction in Patients With Diabetes Mellitus, Hypertension, and Dyslipidemia

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KEYWORDS
Prevention;
Vertigo;
Hearing loss;
Complex disease;
Multifactorial inheritance

Abstract
Introduction and objective: Polygenic or multifactorial inheritance of chronic disorders (MICDs) contributes to irreversible cochleovestibular impairment. Our aim was to determine the type and degree of cochleovestibular dysfunction (CVD) in patients with MICD.
Methods: Cross-sectional. We studied 385 patients with type 2 diabetes mellitus, systemic arterial hypertension and dyslipidemia who were referred to Otorhinolaryngology Unit with hearing and vestibular symptoms. The auditory function was evaluated using conventional tonal audiometry and the vestibular function by electronystagmography. Duration of the disease and number of comorbidities, hearing thresholds at 125–8000 Hz pure tones, speech audiometry, oculomotor evaluation, and thermal caloric tests were also analyzed.
Results: A total of 66.7% (95% CI, 61.8–73.4) of patients had 1 comorbidity; 27.7% (95% CI, 23.3–32.5) had 2 and 5.4% (95% CI, 3.4–8.2) had systemic arterial hypertension, diabetes mellitus, and dyslipidemia. The mean age was 62 years (SD 12.9) and 57.1% were women. The majority showed obesity, physical inactivity and smoking (77.4%; 95% CI, 72.8–81.4). Cochlear dysfunction was more common than CVD (98.9%; 95% CI, 97.3–99.7 versus 36.1%; 95% CI, 31.2–41.1; P < .001). However, the presence of CVD was significant in patients over 60 years (χ² (1, 274) = 6.43, df = 1, P < .01) and with MICD ≥ 11 years old (χ² (1, 274) = 6.43, df = 1, P < .01).

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**Conclusions:** Cochlear dysfunction occurs in patients with MICD and the impact is greater than that of vestibular dysfunction. However, the age factor, duration and number of MICDs contribute to CVD. It is necessary to act on the MICDs and lifestyles to improve CVD. © 2011 Elsevier España, S.L. All rights reserved.

**Disfunción córneo-vestibular en pacientes con diabetes mellitus, hipertensión arterial sistémica y dislipidemia**

**Resumen**

**Introducción y objetivo:** Las enfermedades crónicas de herencia compleja o poligénicas (ECHC) contribuyen al deterioro irreversible córneo-vestibular. Se determinó el tipo y grado de disfunción córneo-vestibular (DCV) en pacientes con ECHC.

**Métodos:** Estudio transversal. Se incluyeron 385 pacientes con diabetes mellitus tipo 2, hipertensión arterial sistémica y dislipidemia que acudieron a otorrinolaringología con síntomas auditivos y vestibulares. La función auditiva se evaluó mediante audiometría tonal convencional y la vestibular por electronistagmografía. Se registró antigüedad y número de comorbididades, umbrales auditivos (125 Hz a 8.000 Hz), logoaudiometría, evaluación oculomotora y pruebas térmicas.

**Resultados:** El 66,7% (IC95%: 61,8 a 71,4) de los pacientes tuvieron un comórbido; 27,7% (IC95%: 23,3 a 32,3) dos y 5,4% (IC95%: 3,4 a 8,2) hipertensión arterial sistémica, diabetes mellitus y dislipidemia. La edad promedio fue de 62 años (DE 12,9) y 56,1% fueron mujeres. La mayoría presentaron obesidad, sedentarismo y tabaquismo (77,4%, IC95%: 72,8 a 81,4). La disfunción cítica fue más frecuente que la DCV (98,9%, IC95%: 97,3 a 99,7 frente a 36,1%, IC95%: 31,2 a 41,1, p = 0,001). Sin embargo, la presencia de DCV fue significativa en pacientes mayores de 60 años (X² tend; p ≤ 0,001, odds ratio: 6,43) y con antigüedad de ECHC ≥ 11 años (X² tend p ≤ 0,001, odds ratio: 4,57).

**Conclusiones:** La disfunción cónica ocurre en pacientes con ECHC y el impacto es mayor que el de la disfunción vestibular. Sin embargo, el factor edad, la antigüedad y el número de ECHC contribuyen a la DCV. Es necesario actuar sobre las ECHC y estilos de vida para mejorar la DCV. © 2011 Elsevier España, S.L. Todos los derechos reservados.

**Introduction**

The importance of polygenic or multifactorial inheritance chronic disorders (MICDs) is illustrated by the level of disability caused by micro- and macrovascular damage occurring at different levels of the organism and by increasing rates of mortality.1 It has recently been established that systemic arterial hypertension (SAH), diabetes mellitus type 2 (DM-2) and dyslipidemia comprise a group of complex genetic disorders (MICDs) which develop through the interaction of environmental and epigenetic factors on the genome of individuals with susceptible allelic variants.2-4 In Mexico, they represent a public health problem7 and for the World Health Organization (WHO) addressing this MICD epidemic has been one of the main challenges of the 21st century.8 MICD contribute to irreversible cochleovestibular and neurological damage; in most cases, functional alterations go unnoticed, are undervalued, underestimated and cause severe disability.9-11 The most severe symptoms are caused by vestibular dysfunction, which generates disability for social and physical activities and an impairment of quality of life.12

Since 1857, an increasing number of experimental studies and clinical trials have offered morphological evidence of cochleovestibular dysfunction (CVD) in the presence of high blood pressure levels, glucose metabolism disorders and elevated lipid levels.9,13,14 Using ultrastructural studies, Tachibana et al. showed that the site of primary lesion by SAH was the stria vascularis of the cochlea, followed by the Corti body.14 In diabetic rats, Perez et al. found alterations in latency and amplitude of the first wave of the vestibular evoked potential, involved in vestibular function.13 Likewise, other studies have shown several pathophysiological mechanisms to explain CVD in these diseases. Among the most significant are an increase in blood viscosity, which subsequently reduces cochleovestibular supply and leads to tissue hypoxia, cellular ionic alterations, which accelerate cochleovestibular degeneration, and abnormalities in the cerebral cortex, which are associated with diffuse microangiopathies affecting the neural sheath of peripheral nerves.9,15 It has also been observed that MICD carriers present bilateral cochlear dysfunction (CD), with a progressive course and affecting high frequencies, similar to the auditory pattern of presbycusis, but with a more severe CD than expected due to age.9,15 However, other studies have not found an association between CVD and MICD and offer conflicting and imprecise results.16,17 There are few studies evaluating CVD in MICD. Recently, an estimation of CD was conducted on the population of Guadalajara, Jalisco, Mexico. This study found that so-called mixed cochleopathy ranked second in frequency among hearing impairments, probably due to a vascular or metabolic factor. However, it also revealed limitations in vestibular symptoms and characteristics of MICD.18 Taking
into consideration that CVD represents irreversible and disabling disorders and that the determinants of MICS can be modified and controlled with preventive recommendations for the improvement of auditory and vestibular function, the present work aimed to determine the type and degree of CVD in patients with DM-2, SAH and dyslipidemia with auditory and/or vestibular symptoms.

Materials and Methods

We conducted a cross-sectional study of all patients with SAH, DM-2, and dyslipidemia who presented auditory and/or vestibular symptoms. These patients volunteered to participate and respond appropriately to an otoneurological evaluation. We excluded those subjects with primary otic diseases or those secondary to infections, noise exposure, ototoxic agents, trauma, tumour, otic surgery, neurological diseases, mental disorders, paroxysmal positional vertigo, Meniere’s disease, vestibular neuritis, and perilymphatic fistula.

Subjects

We consecutively included adult patients of both genders with SAH, DM-2, and dyslipidemia who presented auditory and/or vestibular symptoms. These patients volunteered to participate and respond appropriately to an otoneurological evaluation. We excluded those subjects with primary otic diseases or those secondary to infections, noise exposure, ototoxic agents, trauma, tumour, otic surgery, neurological diseases, mental disorders, paroxysmal positional vertigo, Meniere’s disease, vestibular neuritis, and perilymphatic fistula.

Variables

The criteria for determining MICS included laboratory studies, current prescription of drug treatment and confirmation through medical records. DM-2 was determined according to WHO criteria: levels of >200 mg/dl in random sampling (without fasting) and >126 mg/dl in samples while fasting. SAH was determined according to a recent review of the European Hypertension guide ≥130 mmHg for systolic blood pressure and ≥90 mmHg for diastolic. Dyslipidemia was determined by levels of >220 mg/dl and/or triglycerides >200 mg/dl. Other independent variables included: duration of MICS (1–3, 4–6, 7–9 and >10 years); number of comorbidities (1, 2 or 3 MICS); obesity (body mass index ≥30 kg/m²); smoking, determined by the 20×20 test (do you smoke over 20 cigarettes per day? do you smoke your first cigarette within 20 min of waking up?); drinking, determined by intakes of over 3 ounces per day for men and 1.5 ounces per day for women; sedentary lifestyle—there is no definition for common physical activity; however, we estimated the degree of activity according to 4 sections of daily life (work, transportation, housework, leisure time); coexistence of complications due to MICS (peripheral neuropathy, retinopathy, ischemic heart disease, cerebrovascular disease, renal failure), age, and gender.

We defined as CD cases those patients who did not hear pure tones with an upper intensity limit of 20 dB at frequencies of 125–8000 Hz and an intensity range from 0 to 110 dB. We considered as CVD cases those patients with CD and alterations in oculomotor and/or caloric tests (30 °C and 44 °C); vestibular dysfunction (VD) cases presented normal hearing and alterations in oculomotor and/or caloric tests. VD was determined according to international criteria for the identification of vestibular lesions. Abnormal caloric testing (aCT) was categorized into unilateral and bilateral. These included cases of left or right canalicular hypoflexia, areflexia and hyperreflexia and normal contralateral side. Bilateral cases were those with bilateral vestibular lesion (hypoflexia–hypoflexia, areflexia–hyperreflexia, bilateral areflexia). Canaliculare paresis was defined as ≥22% asymmetry between the left and right responses to the caloric stimulus at 30 °C and 44 °C. Canaliculare areflexia was defined as the absence of canalicular response to the caloric stimulus. Responses were based on the values of subjects without MICS from the population.

Procedure

Patients underwent a clinical evaluation to confirm the existence of MICS. We requested laboratory studies (blood count, biochemistry, urinalysis, electrolytes, lipid profile, and total protein) and blood pressure measurement. We also questioned patients about symptoms of hearing loss, tinnitus, vertigo, and instability, as well as those related with MICS. Subsequently, we conducted a basic ENT examination including rhinoscopy, direct pharyngoscopy, otoscopy, and examination of gait and eye movements.

Subjects also underwent tonal audiometry (TA) using a model 61, GSI (Grason Stadler, Inc.) 2-channel clinical audiometer, calibrated according to ANSI criteria (S3.6-1996), in order to identify auditory thresholds at frequencies 125–8000 Hz, with a gradual intensity of 5 dB. We calculated the mean pure tones at the mentioned frequencies and categorized the hearing level in accordance with the classification issued by the WHO. A speech test was used to corroborate the auditory level in the discrimination of 10 phonetically balanced syllables. For the otoneurological examination we used oculomotor and caloric tests at 30 °C and 44 °C.

We obtained a total sample size of 385 patients and the calculation was conducted using the formula of proportions; the proportion of hearing loss and vertigo cases estimated in consultation was 0.5 (P=0.5), with an accuracy of 5% and a 95% confidence interval (zα=95%, Zα=1.96). The statistical analysis was performed according to the variable measurement scale. Categorical variables were presented as frequencies and proportions (95% confidence intervals [%]). Continuous variables were presented as mean ± standard deviation (SD). The comparison between 2 categorical groups was performed using the Chi-square test. The CVD ratios with respect to the age and duration of MICS groups were estimated through the analysis of linear trend in proportions (χ²trend). The software package used was SPSS v.10 and the value considered for statistical significance was P<.05.

Results

The mean age of the 385 patients was 62 years (SD 12.9) with a minimum of 29 years and a maximum of 88 years. Of
these, 56.1% (95% CI=56.9–61.1) were women. Most suffered 1 comorbidity (66.7%, 95% CI=61.8–71.4), while 27.7% suffered 2 comorbidities (95% CI=23.3–32.5), and 5.4% suffered hypertension, DM-2, and dyslipidemia (95% CI=3.4–8.2). SAH as the only comorbidity and/or with other MICD affected 74.0% (95% CI=69.3–78.3) of the MICD group. On average, patients with 1 comorbidity presented a difference of 7 years compared to those with 3 MICD. Furthermore, dyslipidemic patients had a mean age of 53.3 years (SD 11.6) and presented significant differences with respect to patients with SAH, 2 and 3 comorbidities (P<.01) (Table 1). Hearing loss was the most common symptom (98%, 95% CI=97.3–99.7) and patients with DM-2, 2 and 3 comorbidities were characterized by a high percentage of mixed symptoms. Among the lifestyle factors, patients with DM-2 and dyslipidemia represented the highest percentage of obesity (58.6% and 66.0%). Patients with SAH and 2 comorbidities (35.9% and 45.8%) represented the highest percentage of smokers and physically

Table 1  Percentage Distribution of Symptoms and Lifestyle Factors in (Polygenic) Multifactorial Inheritance Chronic Disorders.

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAH</td>
<td>DM-2</td>
<td>Dyslipidemia</td>
<td>SAH+DM-2 or SAH+Dyslipidemia or DM-2+Dyslipidemia</td>
</tr>
<tr>
<td>n</td>
<td>181</td>
<td>46</td>
<td>30</td>
</tr>
<tr>
<td>Age, years</td>
<td>61.3±12.8</td>
<td>59.2±13.9</td>
<td>53.3±11.6</td>
</tr>
<tr>
<td>Symptoms, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoacusis</td>
<td>98.8</td>
<td>100.0</td>
<td>90.0</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>32.0</td>
<td>78.2</td>
<td>23.3</td>
</tr>
<tr>
<td>Vertigo</td>
<td>29.8</td>
<td>28.2</td>
<td>10.0</td>
</tr>
<tr>
<td>+2 symptoms</td>
<td>42.5</td>
<td>67.3</td>
<td>30.0</td>
</tr>
<tr>
<td>Lifestyle factors, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>19.8</td>
<td>58.6</td>
<td>66.6</td>
</tr>
<tr>
<td>Smoking</td>
<td>35.9</td>
<td>17.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Sedentary life</td>
<td>45.8</td>
<td>34.7</td>
<td>26.6</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>15.4</td>
<td>8.6</td>
<td>13.3</td>
</tr>
<tr>
<td>+2 factors</td>
<td>17.1</td>
<td>21.7</td>
<td>20.0</td>
</tr>
</tbody>
</table>

DM-2: diabetes mellitus type 2; SAH: systemic arterial hypertension.
* P<.01.

Table 2  Cochleovestibular Dysfunction in (Polygenic) Multifactorial Inheritance Chronic Disorders.

<table>
<thead>
<tr>
<th>Variable</th>
<th>20–39 (n=18)</th>
<th>40–59 (n=149)</th>
<th>&gt;60 Years (n=218)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>72.2</td>
<td>73.9</td>
<td>61.2</td>
</tr>
<tr>
<td>2</td>
<td>27.8</td>
<td>22.1</td>
<td>31.9</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>4.0</td>
<td>6.9</td>
</tr>
<tr>
<td>CD, %</td>
<td>100.0</td>
<td>98.6</td>
<td>98.6</td>
</tr>
<tr>
<td>Mild</td>
<td>66.6</td>
<td>52.4</td>
<td>33.3</td>
</tr>
<tr>
<td>Moderate</td>
<td>22.2</td>
<td>27.8</td>
<td>36.5</td>
</tr>
<tr>
<td>Severe</td>
<td>11.2</td>
<td>19.8</td>
<td>28.2</td>
</tr>
<tr>
<td>Deep</td>
<td>0</td>
<td>0</td>
<td>2.0</td>
</tr>
<tr>
<td>CVD, %</td>
<td>11.1</td>
<td>24.8</td>
<td>43.8*</td>
</tr>
<tr>
<td>Spontaneous nystagmus</td>
<td>0</td>
<td>5.4</td>
<td>7.2</td>
</tr>
<tr>
<td>Positional nystagmus</td>
<td>100</td>
<td>56.7</td>
<td>20.8</td>
</tr>
<tr>
<td>Unilateral aCT</td>
<td>100</td>
<td>75.6</td>
<td>70.8</td>
</tr>
<tr>
<td>Bilateral aCT</td>
<td>0</td>
<td>24.4</td>
<td>29.2</td>
</tr>
<tr>
<td>VD, %</td>
<td>0</td>
<td>1.3</td>
<td>0.9</td>
</tr>
</tbody>
</table>

aCT: abnormal caloric test; CD: cochlear dysfunction; CVD: cochleovestibular dysfunction; VD: vestibular dysfunction.
* P<.001.
Cochleovestibular Dysfunction in Patients With Diabetes Mellitus, Hypertension, and Dyslipidemia

Figure 1  Audiograms of vascular-degenerative cochleopathies by conventional tonal audiometry. (a and b) Audiogram of both ears from a 56-year-old woman with SAH+dyslipidemia, the first with an evolution of 20 years; the right ear presented severe sensory hearing loss by PTA/3 and the left ear presented a downward curve with a drop at high frequencies; the ENG was normal. (c and d) Audiogram of both ears from a 47-year-old woman with SAH, with an evolution of 5 years; the right ear showed a superficial hearing loss curve by PTA/3, with a drop in high tones of mixed type with sensory predominance and the left ear presented a normal hearing curve by PTA/3, with a drop at high frequencies of sensory type; the ENG was normal. ENG: electronystagmography; PTA: pure tone average; SAH: systemic arterial hypertension.

Inactive subjects, while patients with SAH represented the highest proportion of alcohol drinkers (Table 1).

Table 2 shows CVD with respect to MICD ordered by age groups. The highest percentage of patients with 1 comorbidity included those aged less than 59 years, while those over 60 years presented the 3 types of comorbidities. Bilateral CD was detected in 98.9% (95% CI=97.3–99.7) of patients and the percentage distribution was uniform across all age groups. A total of 96.8% (95% CI=99.5–98.3) of the audiograms presented downward profile curves, predominantly at high frequencies (4000 and 8000 Hz) (Fig. 1) (descending audiogram). The highest percentages of mild CD were manifested in patients aged less than 59 years, whereas patients over 60 years predominantly manifested moderate
to severe CD. Moreover, patients with DM-2, 2 and 3 comorbidities were characterized by moderate to severe CD (25.7%–41.3%). Up to 40.5% (95% CI=35.5–45.6) of the population underwent electronystagmography due to dizziness, physical unsteadiness and impaired gait. In total, 89.0% (95% CI=35.5–45.6) of the records revealed vestibular dysfunction and 36.1% (95% CI=31.2–41.1) of the population presented CVD. Cases of CVD were more prominent among patients aged over 60 years, with significant differences between age groups (P<.001). In addition, patients with 2 and 3 comorbidities represented the greatest percentage of CVD (53.2% and 57.1%, respectively). VD without cochlear lesion accounted for 1% and was predominant among patients with SAH and 2 comorbidities.

Spontaneous nystagmus was manifested by 2.8% (95% CI=0.7–7.2) of patients and was more frequent in the group aged over 60 years and in patients with SAH and 2 comorbidities. Positional nystagmus was present in the 3 population groups, in particular in patients aged less than 59 years who suffered dyslipidemia. The aCT was unilateral in 73.4% (95% CI=65.2–80.5) of cases and bilateral in 26.6% (95% CI=19.4–34.7). The highest percentage of unilateral aCT was among patients aged under 39 years, whereas the age groups between 40 and <60 years presented similar rates of unilateral and bilateral aCT (Table 2). Up to 35.2% (95% CI=24.0–47.8) of patients with 1 comorbidity presented bilateral aCT.

We verified whether the factors age, number of comorbidities and duration of MICO influenced CVD and determined that the age factor had a greater impact on CVD. The age group >60 years presented a greater risk of CVD compared to the age group 20–39 years (OR=6.43 versus 1.0, $\chi^2_{\text{tend}}\leq0.001$). Furthermore, the risk of CVD was similar with respect to the duration of MICO (OR=4.57 versus 1.0, $\chi^2_{\text{tend}}\leq0.001$) and number of comorbidities (OR=3.56 $\chi^2$, P=0.001) (Table 3). The coexistence of complications derived from MICO affected 43.5% (95% CI=43.4–53.6) of patients. In order of frequency, the following were reported: retinopathy, ischemic heart disease, cerebrovascular disease, diabetic neuropathy, and nephropathy.

### Discussion

The results of this study indicate that CD occurs in patients with MICO and the impact is greater than that of vestibular dysfunction. The risk of developing CVD increases when the factors age (>60 years), duration of MICO and number of comorbidities are added. These results are consistent with similar studies which report that MICO can aggravate age-related hearing loss through their effect on central and peripheral auditory pathways.9,15,21,22 In addition, they also show similarity in micro- and macrovascular complications and lifestyle factors, in particular smoking associated with sensorineural hearing loss.9,15–17,23–25

Hearing loss was the main symptom reported and was related to TA records. This was not the case with vertigo, since it did not appear as a primary manifestation of MICO. Experimental studies have shown that the stria vascularis is a sensitive organ to ischemia, with higher energy requirements compared to the vestibular organ.26 These results may explain the deterioration of the stria vascularis in rats with MICO24,27 and the primary dissociation of cochlear symptoms and vestibular manifestations with a silent and/or delayed presentation in patients with DM and SAH.21 Nevertheless, we believe that the frequency of VD in our study was underestimated because a percentage of the population did not undergo electronystagmography studies due to a lack of vestibular symptoms. We recognize that not all patients with vestibular disease report vertigo and there is evidence of vestibular lesions with and without vertigo.28 Rinne et al.29 noted that the absence of vertigo in vestibular lesions occurred when the disease was bilateral or had a slow evolution. Occasionally, patients only referred dizziness and instability, which delayed the detection of vestibular dysfunction.28 Other authors have described as subclinical vestibular dysfunction and/or incipient inner ear disease that which occurs in patients with vestibular lesions who do not report vertigo, particularly patients with DM-2 and SAH.10,21,28 Brandt et al.30 showed that chronic bilateral dysfunction could be related to hippocampal atrophy and changes in spatial memory, as well as to cerebellar syndromes and autoimmune diseases. Therefore, we believe that patients with MICO who do not present vestibular symptoms or report instability should undergo an otoneurological, neurological and immunological assessment, due to their association with other diseases.28,29

Recently, different types of audiogram have been linked to various diseases and presbycusis.13,14,22,27,31 The studies by Schuknicht correlated presbycusis with the histopathology of the cochlea and various types of audiograms (sensory, neural, conductive cochlear and strial).31 Schuknicht combined the sensory and neural type to refer to sensorineural hearing loss associated with age and affecting the ciliary cells of the base of the cochlea, auditory nerve fibers and spiral ganglion cells. The audiogram would manifest hearing loss at high frequencies. In this article, we have referred to it as a descending audiogram, due to higher auditory records at frequencies of 0.5 kHz at 20 dB than at frequencies of 4 kHz. The cochlear type showed changes in the basilar

### Table 3: Cochleovestibular Dysfunction in Relation to the Age Group, Comorbidities and Duration of (Polygenic) Multifactorial Inheritance Chronic Disorders.

<table>
<thead>
<tr>
<th>Age group</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–39</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>40–59</td>
<td>2.78</td>
<td>0.61–12.66</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>6.42</td>
<td>1.44–28.62</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of comorbidities</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3.04</td>
<td>1.90–4.86</td>
</tr>
<tr>
<td>3</td>
<td>3.56</td>
<td>1.43–8.82</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MICO, years</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>4–6</td>
<td>1.33</td>
<td>0.59–3.00</td>
</tr>
<tr>
<td>7–10</td>
<td>2.12</td>
<td>0.99–4.56</td>
</tr>
<tr>
<td>&gt;11 years</td>
<td>4.57</td>
<td>2.15–9.69</td>
</tr>
</tbody>
</table>

95% CI: 95% confidence interval; MICO: (polygenic) multifactorial inheritance chronic disorders; OR: odds ratio.

$\chi^2_{\text{tend}}\leq0.001$. 

$\chi^2$, P=0.001.
membrane of the cochlea, while the audiogram highlighted middle frequencies with poor discrimination (mean slope audiogram). The strial type was characterized by a degeneration of the stria vascularis affecting all frequencies in the audiogram and was reported as a flat audiogram (auditory records below 20 dB between 0.5 and 4 kHz). In addition, this has been linked with cardiovascular diseases and genetic predisposition. However, Friedland et al. established the ascending audiogram (lower auditory records at frequencies of 0.5 kHz at 20 dB than at frequencies of 4 kHz) as a marker of cardiovascular diseases and a predictor for the prevention of cardiovascular events. This is due to the fact that the stria vascularis is sensitive to ischemia and hearing loss is expressed at low frequencies. In our study, the types of audiogram were consistent with similar studies which revealed ascending audiograms. A minority presented ascending audiograms which could be attributable to vascular disease associated with MICS. 

Systemic Arterial Hypertension and Cochleovestibular Dysfunction

The importance of the stria vascularis in MICS is explained by its vascular anatomy. It is rich in capillaries and fundamental in establishing an endocochlear potential for the propagation of auditory signals to the central nervous system. The arteries which feed it do not contain anastomosis to supplement the blood flow caused by spasms and/or occlusion. The strial capillary network at the apex of the stria is scarce compared to the dense organization of the base. These vascular features make the cochlear apex susceptible to ischemia, reduce the endocochlear potential and lead to the development of significant hearing loss, which can occur immediately after vascular occlusion or anoxia. Experimental studies in rats with SAH showed degeneration of the stria vascularis and descending audiograms. Further studies revealed subcellular changes at the molecular level prior to morphological damage of the stria vascularis. These changes consisted of modifications in the expression of Na, K-ATPase isoforms and increase of endolymphatic K concentration after ischemia. An abnormal K concentration alters the endocochlear potential and causes alterations in auditory records.

There are few clinical studies linking CVD with SAH and they offer controversial results. Esparza et al. showed that patients with SAH aged between 29 and 64 years reported more vertigo and presented descending audiograms, abnormal otoacoustic emissions, and retinopathy compared to patients without SAH. In addition, the responses to caloric tests were not significant between groups. De Moraes Marchiori et al. showed that SAH was a factor that accelerated the degeneration of the auditory system after observing the significant association of hearing loss in patients with SAH. In contrast, Parfenov revealed that vertigo in patients with SAH was not caused by elevated blood pressure, since vertigo occurred in a state of hypotension following the administration of antihypertensive drugs and was associated with neurological and peripheral vestibular diseases and hypotension. Other authors report the deterioration of beta blockers in the function of the inner ear.

Diabetes Mellitus Type 2 and Cochleovestibular Dysfunction

Histological studies of DM-2 have revealed demyelination of the auditory nerve, loss of spiral ganglion cells and ciliated cells of the organ of Corti, degeneration of the central auditory pathways and thinning of vascular walls in the stria vascularis compromising glucose and oxygen supplementation. These conditions evolved to oxidative stress, endolympathic retention hydrops and hearing alterations. Hearing loss was bilateral and progressive, and was more common in DM-2 than in DM-1. The corresponding audiograms were descending and the incipient neuropathic abnormalities were demonstrated through auditory evoked potentials showing prolonged latencies of waves I–IV in the presence of TA and normal vestibular tests. Rozanska-Kudelska et al. demonstrated that DM exacerbates age-related hearing loss by affecting the same frequencies that are damaged by presbycusis in patients with and without DM. Other studies showed that patients with more comorbidities and complications due to DM-2 (retinopathy) had a higher tendency towards CD, since microangiopathy involves both sensory systems (visual and auditory), causing progressive hearing loss and blindness. In contrast, other authors deny the association of hearing loss with retinopathy, neuropathy, and nephropathy. In our study, SAH, DM-2, 2 and 3 comorbidities presented the highest percentages of CVD. This could be attributed to an inner ear circulatory deficit associated with MICS.

Dyslipidemia and Cochleovestibular Dysfunction

Experimental studies with lipid-rich diets have revealed pathological changes in the stria vascularis and external ciliated cells with additive effects in association with SAH and elevated cholesterol. Similarly, low-density cholesterol prevents cochlear blood flow by blocking the production of nitric oxide in the vascular walls. Hypertriglyceridemia and DM-2 increase oxidative stress involved in the pathogenesis of sensorineural hearing loss. However, despite the mechanisms found in dyslipidemia and CD, clinical studies have not been conclusive. Some studies have suggested that hypertriglyceridemia, hypercholesterolemia, and hyperfibrinogenemia diminish cochlear blood flow due to the hyperviscosity and vascular occlusion resulting from atherosclerosis. These additive effects lead to sensorineural hearing loss at high frequencies (2–4 kHz) with susceptibility to noise. In the present study we assumed that the sample size of patients with dyslipidemia as the only comorbidity and associated to other comorbidities was small. Nevertheless, we identified that all presented CD. Furthermore, although CVD in patients with dyslipidemia as the only comorbidity was not demonstrative, we found an additive effect when associated with other comorbidities such as SAH and dyslipidemia, DM-2 and dyslipidemia and/or 3 comorbidities.

One advantage of the study was the estimation in our environment and population of the frequency, type of MICS related to CD and CVD of patients attending otolaryngology services. The lack of auditory evoked potentials to
demonstrate neuropathies and electrystagmography records in the entire population to determine vestibular lesion with and without vertigo were the main disadvantages of the study. Constraints included the type of study design and not excluding subjects over 60 years from the population, which prevented us from inferring cause and effect. Long-term, prospective, randomized studies will be needed to confirm our observations and the many unanswered points. Moreover, studies should be conducted including patients who have recently presented MICD. These would enable an assessment of the period until cochlear and/or vestibular symptoms appear, rather than observations of patients who display complications already attributable to MICD.

Conclusions

Within the group of MICD, SAH represented the highest percentage followed by DM-2. The association of both were the most frequent comorbidities while obesity, smoking and sedentary lifestyle represented the most common lifestyle factors. Thus, although the modification of the latter would not be sufficient to prevent MICD, it is necessary to promote preventive measures in order to improve auditory and visual quality. In addition, studies which analyze whether the modification of these lifestyle factors can prevent CD and/or CVD are required. Bilateral hearing loss was the main symptom, with descending audiograms, whereas vertigo was not the primary manifestation in MICD. Although bilateral CD was found in MICD, this was not the case with vestibular function since most cases presented unilateral CD. In fact, bilateral CD was expected since these are systemic diseases. However, patients who presented bilateral CD were over 40 years and most suffered SAH and 2 comorbidities. Follow-up studies are needed which examine whether the duration of MICD favors bilateral CD, discarding neurological diseases. Age, duration and number of MICD all contributed to the development of CVD.

Conflict of Interests

The authors have no conflicts of interest to declare.

References