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MAIN ARTICLE

Does gestational diabetes result in cochlear damage?

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Abstract

Background: Glucose metabolism has a significant impact on inner-ear physiology. Therefore, hearing may be affected in gestational diabetes.

Method: A matched case–control study was performed to evaluate 27 patients with gestational diabetes and 31 non-diabetic pregnant women with similar demographic characteristics. A medical history was taken for each participant, and otological inspections and high-frequency audiometry tests were performed.

Results: There were no significant differences in average pure tone air–bone hearing thresholds between the groups ($p > 0.05$). However, evaluation of high-frequency hearing thresholds indicated significantly increased auditory thresholds at 10 kHz and 12 kHz for right ears and at 8, 10, 12 and 14 kHz for left ears in the gestational diabetes group ($p < 0.001$).

Conclusion: An investigation into cochlear damage in gestational diabetic patients showed significant high-frequency hearing loss. Further studies are needed to validate these findings in different ethnic groups and geographical populations.

Key words: Diabetes, Gestational; Cochlear Hearing Loss

Introduction

Gestational diabetes mellitus can occur during the second and third trimesters of pregnancy in women who were not diabetic prior to pregnancy. Diabetes mellitus is a genetically determined metabolic disorder associated with absolute or relative impairment in insulin function. It is clinically manifested by metabolic alterations and vascular and neuropathic complications. Gestational diabetes can cause complications in pregnancy similar to those seen in pre-existing diabetes mellitus. The main objective in treating gestational diabetes patients is the prevention of complications.[1]

The inner ear does not store energy, so it is particularly sensitive to altered blood glucose and insulin levels. Minor variations in blood glucose may affect inner-ear function. Altered inner-ear metabolism may lead to auditory and balance disorders; the most common symptoms are vertigo, hearing loss, tinnitus and ear fullness.[2,3] Angiopathy and neuropathy caused by diabetes mellitus are important contributory factors in cochlear dysfunction in diabetic patients.[1,4]

Although diabetes mellitus often results in hearing impairment, there is little data to indicate whether gestational diabetes is an antenatal risk factor for cochlear damage and hearing loss. This study aimed to investigate whether gestational diabetes results in cochlear damage and thus sensorineural hearing impairment. To our knowledge, no previous study has addressed this question.

Materials and methods

Patients

We studied 27 women with gestational diabetes and 31 pregnant controls with normal glucose tolerance between September 2012 and April 2013. Because women with gestational diabetes are generally overweight compared with women with normal pregnancies, only women with a body mass index (BMI) greater than 25 kg/m^2 were included in the control group.

Gestational diabetes was diagnosed using a 2-hour oral glucose (50 g) tolerance test, according to World Health Organization and modified International Association of Diabetes in Pregnancy Study Group criteria. Cut-off values were more than 5.2 mmol/l glucose in the fasting state, more than 10.0 mmol/l after 1 hour and more than 7.8 mmol/l after 2 hours.[5] HbA1c levels were measured by an immunoturbidimetric assay using a COBAS Integra 800 system (Roche Diagnostics, Basel, Switzerland): intra- and inter-assay coefficients of variation were 0.8–1.3 per cent. The methodology conformed to Diabetes

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Control and Complications Trial and National Glycohemoglobin Standardization Program standards. A HbA1c level of more than 7 per cent was accepted as the cut-off value for elevated HbA1c.[5] Gestational diabetes was diagnosed for fasting plasma glucose concentrations greater than 7.0 mmol/l or HbA1c levels greater than 7 per cent.

A low-calorie diet (1600–1800 kcal/day) was started immediately after diagnosis of gestational diabetes. Insulin treatment was initiated if, despite the strict diet, fasting blood glucose met or exceeded 5.5 mmol/l or postprandial glucose 1 h after a meal was greater than 7.8 mmol/l. Women in the non-diabetic pregnant group had no history of pathological blood glucose values or previous gestational diabetes. Similar to those in the gestational diabetes group, they were overweight and aged between 18 and 40 years. Exclusion criteria for the study were a history of ear disease, previous sensorineural hearing loss (SNHL), more than 40 years of age and taking any medication that affects glucose metabolism (e.g. systemic corticosteroids). Patients at less than 32 weeks of gestation were excluded from the study. This was done so that the effects of dysregulated glucose metabolism on the inner ear could be studied. All clinical assessments were performed by the same investigator and all audiometric evaluations were assessed by the same audiometrist.

The study was approved by the Institutional Research Ethics Committee. Patients gave informed consent before undergoing the following procedures.

Clinical history

A questionnaire was used to obtain information on oto-neurological signs and symptoms, and both personal and family medical history. Patients with diseases other than diabetes were excluded.

Otorhinolaryngological evaluation

This evaluation was performed to exclude conditions that might interfere with auditory tests.

Audiological evaluation

Conventional pure tone and high-frequency audiometry was performed using an Interacoustics AC 40 audiometer and TDH 39P earphones; thresholds were given in dB. Bone and air conduction thresholds were measured at 0.25, 0.5, 1, 2, 4, 8, 10, 12, 14 and 16 kHz. The speech recognition threshold and rate were measured in an acoustic booth to avoid interference from extraneous noise. Bone and air conduction thresholds of 0.5, 1, 2 and 4 kHz were used to calculate average pure tone air–bone hearing thresholds.

Participants underwent another hearing threshold evaluation three to four weeks after childbirth.

Statistical analysis

All analyses were carried out using PASW software, version 18.0 for Windows (formerly SPSS, Chicago, Illinois, USA), and the Mann–Whitney U test, student's *t*-test and Wilcoxon's signed rank test.

Results

The study population comprised 27 women with gestational diabetes and 31 non-diabetic pregnant women; 3 candidates were excluded because of tympanic membrane perforation or conductive hearing loss. Interviews were held at median gestational week 33.2 ± 1.3 (range 32.1–34.7 weeks) in the study group and at median gestational week 32.9 ± 1.5 in the control group (range 31.3–33.8 weeks).

There were no significant differences in baseline characteristics such as age, duration of pregnancy and BMI between women with gestational diabetes and non-diabetic pregnant women. Gestational diabetes patients were aged between 21 and 39 years (mean age 28.4 ± 4.7 years) and control participants were aged between 19 and 40 years (mean age 29.4 ± 5.2 years). Women with gestational diabetes had slightly higher BMIs compared with controls (29.2 *vs* 28.6 kg/m^2, $p > 0.05$). Five women in the gestational diabetes group (18.5 per cent) needed insulin in addition to dietary treatment.

No differences between groups were observed in tympanic membrane status or other otolaryngological parameters. The average pure tone air–bone hearing threshold was 0–5 dB for the left ear and 0–7 dB for the right ear in the gestational diabetic group, and 0–5 dB for the left ear and 0–5 dB for the right ear in the non-diabetic pregnant group. There was no significant difference in average pure tone air–bone hearing thresholds between the groups (*p* values were greater than 0.05).

A positive correlation was found between average hearing thresholds and the results of a 50-g glucose oral glucose tolerance test (at fasting and after 1, 2 and 3 hours).

Average pure tone bone conduction hearing thresholds in both groups are shown in Table I. Audiological tests revealed significant sensorineural hearing differences at two frequencies for the right ear (10 and 14 kHz), and at four frequencies for the left ear (8, 10, 12 and 14 kHz; $p < 0.01$). Rates of hearing loss at each frequency for both ears in both experimental groups are shown in Table I. Audiological findings for right and left ears in both groups are shown in Figures 1 and 2, respectively.

After childbirth, 21 out of 27 women with gestational diabetes were available for audiological re-evaluation; 6 patients dropped out of the study. For the 21 patients, audiological data in the second tests were almost the same as in the first evaluation. There was no significant difference in hearing threshold at any frequency for both ears between gestational and post-delivery values (*p* values were all greater than 0.05).

Discussion

Aetiological classification of glucose disorders by the World Health Organization is based on research

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TABLE I
AVERAGE PURE TONE BONE CONDUCTION HEARING THRESHOLDS IN GESTATIONAL DIABETIC AND NON-DIABETIC PREGNANT GROUPS

	Control group (n=31)		GDM group (n=27)		p value
Frequency (kHz)	Mean ± SD (dB)	Range (dB)	Mean ± SD (dB)	Range (dB)	
Right ear					
0.25	8.3 ± 5.2	5–20	8.1 ± 6	5–25	0.067
0.5	7.9 ± 4.03	5–20	7.4 ± 5.6	5–25	0.139
1	7.9 ± 6.9	5–40	6.6 ± 3.1	5–15	0.743
2	7.1 ± 4	5–20	6.5 ± 3.9	5–20	0.411
4	5.8 ± 3.8	0–20	6.1 ± 2.8	5–15	0.242
8	9.6 ± 6.1	5–35	19 ± 16.5	5–50	0.82
10	9.5 ± 6.5	5–15	20.9 ± 13	10–30	<0.001
12	17.9 ± 14.4	5–35	31.6 ± 24.6	15–40	0.018
14	19.8 ± 20.5	5–30	37.7 ± 21.3	20–60	<0.001
16	34.3 ± 26.6	10–70	46.1 ± 20	30–70	0.059
Left ear					
0.25	9 ± 6.6	5–30	8.5 ± 6.4	5–25	0.888
0.5	7.7 ± 5.4	5–30	8.3 ± 6.6	5–30	0.923
1	7.9 ± 6.8	5–40	7.04 ± 6.08	5–30	0.227
2	6.6 ± 4.3	5–25	6.7 ± 3.2	5–15	0.460
4	6.9 ± 4.9	5–30	6.9 ± 5	5–25	0.608
8	6.6 ± 3.7	5–15	19.2 ± 13.6	5–25	<0.001
10	9.5 ± 6.2	5–15	22.5 ± 12.1	10–30	<0.001
12	19.5 ± 17	5–35	40.5 ± 23.3	20–60	<0.001
14	20.1 ± 18.4	5–35	43.8 ± 20	25–60	<0.001
16	33.2 ± 24.5	15–60	50.9 ± 15.8	40–60	0.007

GDM = gestational diabetes mellitus; SD = standard deviation

performed by the National Diabetes Data Group. This group suggested classifying diabetes mellitus and other states of glucose intolerance into three subclasses: type 1, type 2 and secondary diabetes associated with another identifiable condition or syndrome.[6,7] Gestational diabetes frequently precedes type 2 diabetes. Two large meta-analyses on type 2 diabetes development following gestational diabetes report a risk ratio of 7.43 and cumulative incidence rates of up to 70 per cent.[8,9]

Gestational diabetes is a metabolically heterogeneous disorder. However, when high fasting blood glucose values are found, treatment with basal insulin is compulsory. We also managed the disease using either dietary regulation or insulin treatment.

Various studies have shown that the cochlear system may be altered in diabetic patients; about 24 per cent of diabetic patients have impaired hearing.[10] Many clinical trials have revealed a relationship between hearing loss and diabetes. For example, a recent meta-analysis on the association of diabetes mellitus with hearing alterations showed type 2 diabetic patients to have a significantly higher incidence of at least mild hearing loss.[11] In a study by Ozel *et al*., hearing thresholds at all frequencies (except for 0.5 kHz for bone conduction) and speech recognition scores values were

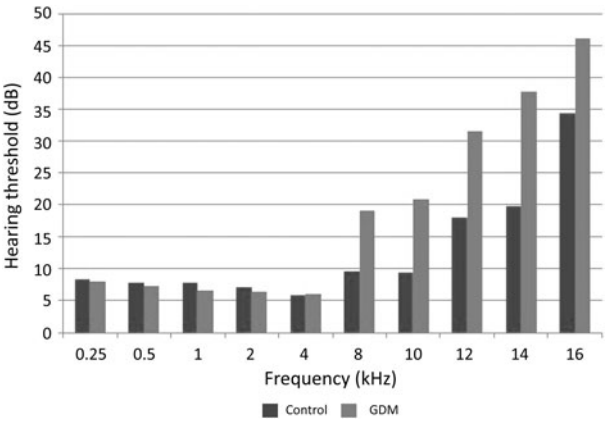

FIG. 1
Average pure tone bone conduction hearing thresholds for right ears in gestational diabetic group and non-diabetic pregnant group. GDM = gestational diabetes mellitus

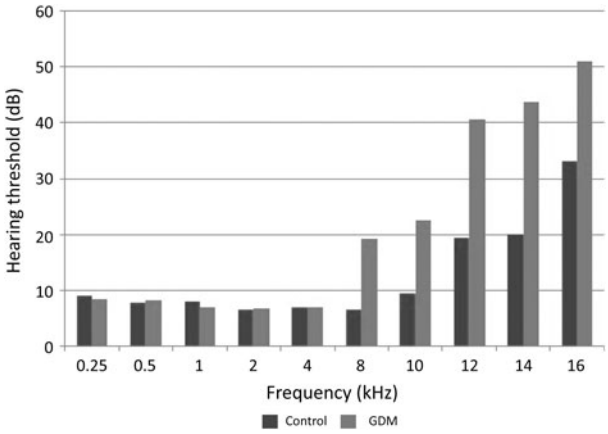

FIG. 2
Average pure tone bone conduction hearing thresholds for left ears in gestational diabetic group and non-diabetic pregnant group. GDM = gestational diabetes mellitus

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significantly lower in patients with diabetes mellitus than in control participants.[12] Biurrun *et al*. identified 11 cases (23.9 per cent) of mild SNHL, mostly at high frequencies, with no associated auditory complaints.[13] These studies have established inner-ear vessel involvement and alterations to vascular striae in diabetic patients, strongly suggesting a causative link between diabetes and hearing loss.

The auditory system requires high glucose levels because of the high energy utilisation of its complex signal processing activity. Hearing loss in the context of type 2 diabetes may result from microangiopathic processes that follow glucoprotein deposition caused by hyperglycaemia in small blood vessels, which affects neurological function.[14] Peripheral neuropathy, nephropathy and retinopathy in diabetes are known to result from this microangiopathic process. A number of possible physiological mechanisms have been proposed to explain the link between hearing loss and type 2 diabetes. These include vascular and neurological aetiologies, including effects of diabetes on the central nervous system, in addition to mitochondrial abnormalities and genetic causes.[4,14,15] While many studies have reported distinct effects of type 2 diabetes on the auditory system, none have investigated the effects of gestational diabetes on the auditory system. Recognised maternal complications of gestational diabetes include an increased risk of developing type 2 diabetes, metabolic syndrome and cardiovascular diseases.[16,17] Altered glucose metabolism in pregnancy may influence inner-ear physiology to resemble that seen in diabetic patients.

- **Gestational diabetes may cause hearing alterations similar to those seen in diabetes mellitus**
- **Diabetes mellitus causes cochlear dysfunction mainly via angiopathy and neuropathy**
- **There was no significant difference in average pure tone air–bone hearing thresholds between diabetic and non-diabetic pregnant women**
- **Significant high-frequency hearing loss in gestational diabetic patients suggests cochlear dysfunction**

Audiological tests revealed significant SNHL at two frequencies for right ears (10 and 14 kHz), and at four frequencies for left ears (8, 10, 12 and 14 kHz) in gestational diabetics compared with controls. Maia and Campos described severe atrophy of the spiral ganglion associated with loss of cells of the basal and medium turns of the cochlea, in addition to a decreased number of nerve fibres in the spiral lamina.[1] Loss of cells in the basal turn of the cochlea may explain the high-frequency hearing loss observed in our study.

As the inner ear is vulnerable to metabolic and circulatory stress, it is logical to expect microvascular complications of gestational diabetes to affect the auditory system. Gestational diabetes may result in hearing loss to a similar extent to that seen in diabetes mellitus. However, a robust evaluation of hearing loss associated with gestational diabetes requires larger study populations and additional research focusing on the mechanism of the pathology.

Conclusion

There were no significant differences in average pure tone air–bone hearing thresholds between gestational diabetic and non-diabetic pregnant groups ($p > 0.05$). However, high-frequency hearing threshold audiometry revealed significant high-frequency hearing loss in gestational diabetic patients, suggesting cochlear dysfunction.

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