

Is Preeclampsia a New Risk Factor for Cochlear Damage and Hearing Loss?

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Objective: We investigated whether preeclampsia is a risk factor for cochlear damage and permanent hearing loss.

Study Design: Prospective case-control study design.

Setting: Academic tertiary medical center.

Patients: Subjects included 40 patients with preeclampsia and 30 healthy pregnant women.

Interventions: Oscopic examinations and pure-tone audiometry, tympanometry, otoacoustic emissions (OAEs), and stapedial reflex tests were conducted for all subjects. Negative audiologic tests were reevaluated after the postpartum period. Statistical analyses were performed using χ^2 and binary logistic regression testing.

Main Outcome Measures: We searched for signs of middle ear ventilation, damage of cochlea, and sensorineural hearing loss.

Results: Eight patients from the preeclampsia group had 1 or more otological problems. Two patients from the control group were determined as having otological problems. Otoacoustic emissions of the right and left ears ($p = 0.029$, $p = 0.044$), hearing levels of right and left ear bone conduction (BC) at

the 500-Hz frequency (right and left–BC 500), and left ear at the 2,000-Hz frequency (left–BC 2000) differed significantly between the preeclampsia and control groups ($p = 0.040$, $p = 0.003$, and $p = 0.003$). There was no significant difference in the OAEs between the right and left ears in the preeclampsia group ($p < 0.05$). The variables BC 500–left, BC 500–right, OAE-right, and OAE-left differed significantly between groups based on binary logistic testing. The odds ratio and 95% confidence intervals (95% CI) for these 4 risk variables were as follows: BC 500–left, 1.167 (1.044–1.306); BC 500–right, 1.117 (1.002–1.244); OAE-right, 0.642 (0.505–0.815); and OAE-left, 0.576 (0.475–0.698), respectively.

Conclusion: Preeclampsia is a risk factor for cochlear damage and permanent hearing loss. Even if preeclampsia resolves after delivery, cochlear damage and permanent hearing loss remain unchanged in patients with preeclampsia. **Key Words:** Hearing loss—Otoacoustic emissions—Preeclampsia.

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Vascular lesions, viral infections, and immune reactions might all play roles in damage to the inner ear. Immune reactions do not always have a negative effect on the inner ear, but because the inner ear is very susceptible to external and internal factors, immune regulation is very important to the limited regeneration ability of the inner ear. Systemic illness may also damage the inner ear (1,2).

Preeclampsia is a disease characterized by hypertension and large quantities of protein in the urine during pregnancy. Preeclampsia occurs in approximately 5% to 7% of all pregnancies and is a major cause of maternal morbidity and mortality (3). Inadequate cytotrophoblast invasion of placenta, maternal endothelial dysfunction, and placental antiangiogenic factors can all play roles in the pathogenesis of preeclampsia. Placental antiangio-

genic factors can be released into the maternal circulation and can disrupt the maternal endothelium, resulting in hypertension, proteinuria, and other systemic manifestations of preeclampsia (4). The heart, eyes, and/or kidney of preeclampsia patients can be negatively affected by ischemia, vasoconstriction, and autoimmune reactions. Although the inner ear is vulnerable to the same conditions, little is known about how it can be affected by preeclampsia. To the best of our knowledge, the only published study on this subject is that by Bakhshae et al. (5) where they evaluated whether otoacoustic emissions (OAEs) were present in preeclamptic pregnancies, but no research was made into hearing thresholds. The study concluded that preeclampsia might be a risk factor for the inner ear.

Because preeclampsia is a clinical occurrence affecting a large proportion of pregnancies, the prevention of complications that may result in preeclampsia is important from the aspect of morbidity and mortality. Several studies

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have addressed the problem of preeclampsia in the area of nephrology, ophthalmology, cardiology, and neurology but not in otology. The aim of this study was to determine whether preeclampsia was a risk factor from an otological aspect and, by drawing attention to this subject, to establish what preventative and precautionary measures should be taken from an otological aspect.

MATERIALS AND METHODS

This prospective study was conducted between January 1, 2008, and December 31, 2009, in the Otolaryngology and Obstetrics–Gynecology Departments. Informed consent was obtained from all participants. Subjects included 30 healthy pregnant women as controls and 40 women with preeclampsia, defined by the presence of a maternal blood pressure higher than 140/90 mm Hg after 20 weeks of gestation and proteinuria of at least 300 mg/24 h. The hearing test, blood pressure measurement, and urine test were performed on the same days. The preeclamptic and healthy pregnant women were all being monitored by clinical obstetricians. Patients with renal disease, chronic hypertension, diabetes or other metabolic disorders, thyroid malfunction, a rheumatologic disorder, a history of ototoxic drug consumption, twin pregnancies, a maternal age older than 40 years, a history of ear disease, or a temporal bone fracture were excluded from the study.

Otoscope examinations were conducted for all participants. Hearing thresholds were assessed using the Clinical Audiometer AC33 (Interacoustics A/S, Assens, Denmark). In addition, bone and airway conduction thresholds were measured at frequencies of 250, 500, 1,000, 2,000, 4,000, and 8,000 Hz. The outer ear canal volume, membrane compliance, gradient, and pressure parameters were recorded using the Clinical Impedance Audiometer AZ26 (Interacoustics). Tympanometry results were classified into Types A, B, and C, as set out by Liden (6) and Jerger (7). Stapes reflex was also recorded using the Clinical Impedance Audiometer AZ26 (Interacoustics). Cochlear function was evaluated by measuring transient evoked OAEs from 1,000 to 4,000 Hz at an intensity of 80 ± 3 dB using an OAE device (ILO288; Interacoustics).

Statistical Analysis

Mean and SDs were calculated for continuous variables. The normality of the variables was analyzed by Kolmogorov–Smirnov test. Associations between the categorical and continuous variables were evaluated using χ^2 test with the Yates correction and the Student *t* test. Logistic regression method

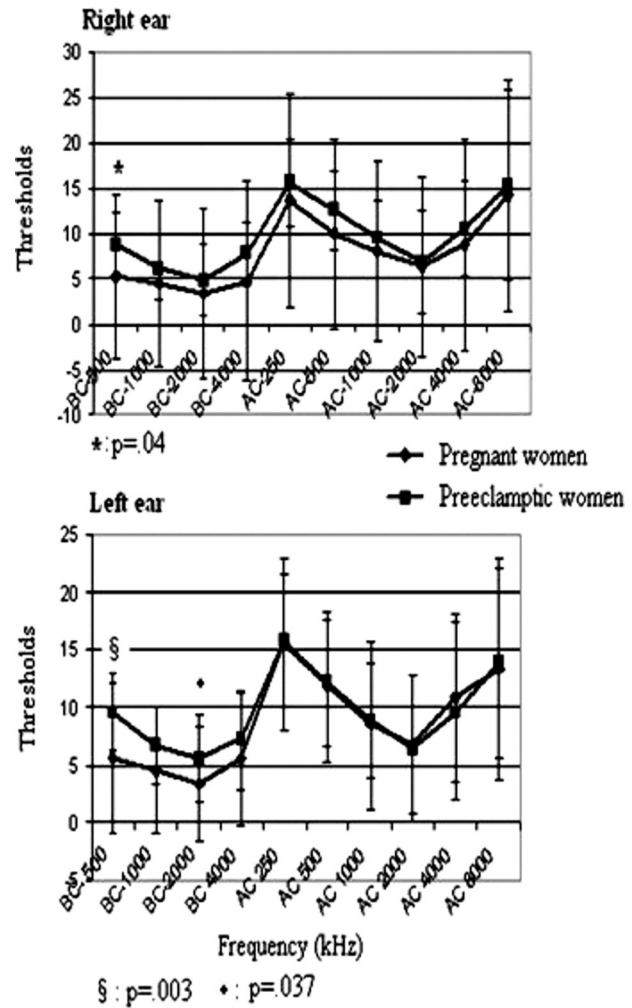


FIG. 1. Comparison of bone and airway thresholds in preeclamptic and control patients. Vertical short lines indicate SD.

was performed to find the risk variables for patients with preeclampsia by including all variables in the model. Odds ratios were calculated by logistic regression method. All variables were included in the backward stepwise procedure. Two-sided *p* values were considered statistically significant at *p* < 0.05. Statistical analyses were performed/conducted using the

TABLE 1. Comparison of preeclamptic and control cases

	Control pregnant women (n = 30)	Preeclamptic women (n = 40)	χ^2	<i>p</i>
Tympanic membrane abnormality (right)	0	1	0.001	0.999
Tympanic membrane abnormality (left)	0	0	—	—
Abnormal tympanometry (type b–c) (right)	0	2	1.506	0.471
Abnormal tympanometry (type b–c) (left)	1	0	0.025	0.875
Stapedial reflex (right)	0	4	1.538	0.078
Stapedial reflex (left)	1	2	0.001	0.999
OAE (right)	0	8	4.79	0.029 ^a
OAE (left)	0	7	4.05	0.044 ^a
Abnormal otologic findings	2	8	—	—

^a*p* < 0.05.

TABLE 2. *The outcomes of binary logistic regression model for all of the patients*

Variable	β	SE	Odds Ratio (95% CI)	WALD	<i>p</i>
BC 500–left	0.155	0.057	1.167 (1.044–1.306)	7.355	0.007 ^a
BC 500–right	0.110	0.055	1.117 (1.002–1.244)	3.980	0.046 ^a
OAE-right	-0.443	0.122	0.642 (0.505–0.815)	13.18	<0.001 ^a
OAE-left	-0.551	0.098	0.576 (0.475–0.698)	31.61	<0.001 ^a

β indicates coefficient of regression; SE, standard error of β .

^a*p* < 0.05.

statistical packages for SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL, USA).

RESULTS

The preeclampsia group included 40 women (mean age, 31.43 ± 7.62 yr; range, 19–36 yr) and the control group included 30 women (mean age, 29.66 ± 6.95 yr; range, 20–34 yr). At the time of the tests, all the pregnancies were 20 weeks or more. Eight of the preeclampsia patients had 1 or more otological problems. In 2 women from the control group, otological abnormalities were detected. No differences were observed between the 2 groups in tympanic membrane status, tympanometry type, and stapedial reflex. The 2 groups differed significantly in right and left ear OAEs (*p* = 0.029 and *p* = 0.044, respectively; Table 1). However, in the preeclampsia group, there was no significant difference in the OAEs between the right and left ears (*p* > 0.05). The 2 groups also differed significantly in hearing thresholds of right and left ears at BC 500, and left ears at BC 2000 differed significantly (*p* = 0.040 and *p* = 0.003, respectively; Fig. 1). Subjects were rechecked 3 to 4 weeks after delivery of the placenta for an additional emission measurement and evaluation of hearing thresholds. Negativity for OAE and a decrease in hearing thresholds at low frequency were observed to continue. Risk variables in women with preeclampsia were obtained using the logistic regression method. Table 2 presents the results of the logistic method. The method revealed that the following variables were significant: BC 500–left, BC 500–right, OAE-right, and OAE-left. The odds ratios and 95% confidence intervals (95% CIs) for these 4 risk variables were as follows: 1.167 (1.044–1.306), 1.117 (1.002–1.244), 0.642 (0.505–0.815), and 0.576 (0.475–0.698), respectively.

DISCUSSION

The underlying mechanisms of preeclampsia are not fully understood. However, placental hypoperfusion is present in the cause, and this leads to an increase in placental factors (soluble tyrosine kinase 1 and antiangiogenic factors such as soluble endoglin) and a decrease in placental growth factor and vascular endothelial growth factor (proangiogenic factors) (8,9). An imbalance of antiangiogenic factors is thought to trigger vascular endothelial cell injury in the liver, kidney, and brain, as well as within the placenta itself (10). In addition,

increased vascular resistance and diffused or segmental multifocal vasospasms have been reported in cases of preeclampsia (11,12). These clinical factors most likely result in hypertension, proteinuria, and other systemic manifestations of the syndrome. Traditionally, preeclampsia has been viewed as a self-limited condition that resolves after delivery of the placenta. However, recent research has shown that maternal endothelial dysfunction may persist for years after the episode (10).

The inner ear is known to be easily affected by systemic incidents, especially vascular, immune, and metabolic changes. Basic physiopathologic finding in preeclampsia includes vasospasm, vasculopathy, immunological factors, and inflammatory changes. Therefore, preeclampsia probably has a negative effect on the inner ear and hearing thresholds. Bakhshae et al. (5) evaluated transient OAEs and found that the preeclamptic and control groups differed significantly, but they found no significant differences between the 2 groups 2 weeks after delivery at follow-up. However, it was provisionally stated that not taking transient OAE shows that preeclampsia could be a risk factor in cochlear damage. Our study differed from the research of Bakhshae et al. (5) in that we evaluated hearing threshold, stapes reflex, and tympanometry in addition to OAEs. We found bilateral failure in cochlear function in patients with preeclampsia. This failure was particularly affected by low frequencies, so a drop in hearing threshold seemed to arise in bone conduction at low frequencies. This failure continued after delivery. The fact that we determined hearing loss in low frequencies supports the notion that vascular and immune components play an important role in the preeclampsia-induced otopathologic abnormality. We hypothesize that the low-frequency hearing loss reflects the areas of the inner ear affected by ischemia. We think that the hearing loss at low frequency depends on these ischemic areas, particularly the affected cochlear apical section because this seems to be more sensitive to vascular and immunological incidents. Sennaroglu and Belgin (13) determined a loss of hearing at low frequency in their study of healthy pregnancies, but the hearing returned to normal after the birth. This hearing loss at low frequency during pregnancy was stated to be the result of fluid and electrolyte accumulation, thus resembling the loss of hearing at low frequency of Ménière's disease. In a study by Masutani et al. (14) where vascular damage was experimentally created, vascular deficiency was determined as developing particularly in the cochlear apical section. Taking these studies into consideration, we speculated that in patients with preeclampsia, endolymphatic hydrops developed after microvascular circulation deficiency, and this could be the reason for the loss of hearing at low frequencies. However, no symptoms of Ménière's disease were determined in our study.

Preeclampsia resolves after delivery. However, complications that result from preeclampsia may be permanent. The evaluations performed/conducted 3 to 4 weeks after the birth showed the hearing damage to have continued. It is thought that despite the resolution of

preeclampsia symptoms, if there has been damage to the hearing, the resultant loss of hearing is permanent.

Logistic regression testing revealed a significantly increased risk for hearing loss in patients with preeclampsia. Among our study population, even if the preeclampsia resolved, hearing damage was permanent, and preeclampsia was a risk factor for cochlear damage and hearing loss.

There are varying results reported from studies in literature that evaluate the hearing of babies from preeclamptic pregnancies. Wells (15) and Withagen et al. (16) found no risk of hearing loss in babies born to patients with preeclampsia. Bakhshaei et al. (17), in an evaluation of babies from healthy and preeclamptic pregnancies, found a significant difference between the 2 groups on the first scan of OAE, but on the second follow-up of auditory brainstem response and OAE, no difference was determined between the 2 groups. In a large series studied by Wells (15), it was stated that preeclampsia was not a risk factor for infant hearing loss. The same study reported 1 case of extensive inner ear damage determined from the temporal bone specimen at the postmortem of a baby born to a mother with preeclampsia. These studies show that hearing may be affected in babies born to mothers with preeclampsia.

In conclusion, patients with preeclampsia may experience failure in inner ear function and hearing threshold. Preeclampsia might damage ear function, so every patient with preeclampsia should also be evaluated by an otolaryngologist throughout her treatment and follow-up.

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