

# Association of NIDDM and Hearing Loss

DAYNA S. DALTON, MS  
KAREN J. CRUICKSHANKS, PHD  
RONALD KLEIN, MD

BARBARA E.K. KLEIN, MD  
TERRY L. WILEY, PHD

**OBJECTIVE** — To evaluate the association of NIDDM with hearing loss in a large population-based study.

**RESEARCH DESIGN AND METHODS** — Data from population-based longitudinal studies of aging conducted in Beaver Dam, Wisconsin, were used in these analyses. Hearing thresholds were determined by pure-tone air- and bone-conduction audiometry performed by trained technicians following American Speech-Language-Hearing Association specifications. Hearing loss was defined as the pure-tone average of the frequencies 500, 1,000, 2,000, and 4,000 Hz greater than 25 decibels hearing level in the worse ear. Diabetes status was determined by self-report of physician-diagnosed diabetes or by elevated glucose or glycated hemoglobin levels at examination.

**RESULTS** — Of 3,571 study participants, 344 were classified as having NIDDM. Subjects with NIDDM were more likely to have a hearing loss than were subjects without diabetes (59 vs. 44%). After results were adjusted for age, this difference was not statistically significant. After individuals with hearing loss patterns inconsistent with presbycusis were excluded, there was an association between NIDDM and hearing loss when controlling for potential confounders (odds ratio [OR] 1.41, 95% CI 1.05–1.88). There was no association between duration of diabetes or glycemic control and hearing loss. Individuals with NIDDM and nephropathy were more likely to have a hearing loss than were those with NIDDM but no nephropathy (OR 2.28, 95% CI 1.04–5.00).

**CONCLUSIONS** — These data are suggestive of a weak association between NIDDM and hearing loss.

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**N**IDDM and age-related hearing loss are both very common conditions affecting the health and quality of life of older adults (1,2). NIDDM is associated with a number of microvascular complications affecting most commonly the eyes and kidneys of individuals with diabetes. It has been postulated that microvascular abnormalities may also affect the ears and hearing of individuals with diabetes. Studies in diabetic animals have demonstrated thickening of the basement membrane of the capillaries of the stria vascularis (3).

Histopathological studies have shown damage to the nerves and vessels of the inner ear of individuals with diabetes (4–7). These vascular lesions have been theorized to be an important causative factor for neuronal degeneration in the auditory system.

A number of clinical studies have investigated the possible association of diabetes and hearing loss (8–20). Most of these previous studies were very small, evaluating 20–50 subjects (10,11,13,15–19), which may have limited the ability to detect any association. Only one of these studies eval-

uated NIDDM specifically (14), and several others did not differentiate between IDDM and NIDDM (8–10,12,14,16). In the studies using a comparison group (9–20), information regarding the selection of the comparison group is lacking (11,13–15, 17–20), or the selected group consists of medical personnel (10) or groups with significant noise exposure (9,16). These limitations have contributed to inconsistent results in the literature. The larger studies, with 99–200 participants (9,12,14), failed to find an overall association between diabetes and hearing loss, but in two of these studies (9,12), hearing loss was found to be associated with nephropathy and severe retinopathy.

Only one population-based study, the Framingham Heart Study, has evaluated the association between diabetes and hearing loss (21). Using audiometric data obtained at biennial examination 18, pure-tone averages (PTAs) were calculated for the frequencies of 0.25, 0.5, and 1 kHz (PTA lo) and 4, 6, and 8 kHz (PTA hi). No association was found between hearing thresholds and the presence or absence of diabetes or impaired glucose tolerance. However, PTA lo was associated with blood glucose in women, suggesting that hearing thresholds increased (became worse) as blood sugar increased.

Although the animal studies and pathology series suggest a plausible biological basis for an association between diabetes and hearing loss, the results of the previous clinical studies and the single population-based study have been equivocal. The purpose of this article is to evaluate the association of diabetes with hearing loss in a large, population-based study.

## RESEARCH DESIGN AND METHODS

Data for these analyses come from the Epidemiology of Hearing Loss Study (EHLS) (2) and the Beaver Dam Eye Study (BDES) (22), which are population-based, longitudinal studies of age-related sensory disorders conducted in Beaver Dam, Wisconsin. A private census of the city and township of Beaver Dam conducted from September 1987 to May 1988 identified 5,924 residents in the target age range of 43–84 years. Of these, 4,926 (83%) participated in the baseline eye examination conducted from March 1988

From the Department of Ophthalmology and Visual Sciences (D.S.D., K.J.C., R.K., B.E.K.K.) and the Department of Communicative Disorders (T.L.W.), University of Wisconsin, Madison, Wisconsin.

Address correspondence and reprint requests to Dayna S. Dalton, MS, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, 610 North Walnut St., 460 WARF, Madison, WI 53705-2397. E-mail: dalton@epi.ophth.wisc.edu.

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**Abbreviations:** BDES, Beaver Dam Eye Study; dB HL, decibels in hearing loss; EHLS, Epidemiology of Hearing Loss Study; OR, odds ratio; PTA, pure-tone average.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

through August 1990; 337 (5.6%) refused the examination but agreed to be interviewed; 18 (0.3%) could not be located; 226 (3.8%) died; and 417 (7%) refused.

The first examination phase of the EHLS ran concurrently with the 5-year follow-up BDES examination (1993–1995). Individuals who participated in the baseline eye examination and who were still living as of March 1, 1993, were eligible for the EHLS. Of the 4,541 eligible people, 3,571 (79%) were examined by the hearing study; 182 (4%) refused the examination but agreed to be interviewed; 4 (0.1%) could not be located; 180 (4%) died before participating; and 604 (13%) refused.

Three trained technicians (one a certified clinical audiologist) performed the hearing examinations. The examination included an otoscopic evaluation (23), a screening tympanogram (GSI 37 Autotymp; Lucas GSI, Littleton, MA) (23,24), and pure-tone air- and bone-conduction audiometry. The audiometric testing was conducted using Virtual 320 clinical audiometers (Virtual Corporation, Seattle, WA) equipped with TDH-50 earphones in sound-treated booths (IndustrialAcoustics, New York, NY) following American Speech-Language-Hearing Association guidelines (25). Insert earphones (E-A-Rtone 3A; Cabot Safety, Indianapolis, IN) and masking were used as necessary. Ambient sound levels were routinely monitored to ensure compliance with maximum permissible levels (26). Pure-tone air-conduction thresholds were obtained for each ear at 250, 500, 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz. Bone-conduction thresholds were measured at 500 and 4,000 Hz. A portable audiometer (Belton 112; Electronic, Chicago) was used to test participants who were not able to travel to the clinic site ( $n = 132$ ). All audiometric equipment complied with American National Standards Institute (ANSI) specifications (27) and was re-calibrated every 6 months throughout the study period.

The PTA of the thresholds at 500, 1,000, 2,000, and 4,000 Hz was calculated for each ear. Hearing loss was defined as a PTA of  $>25$  decibels hearing level (dB HL) in the worse ear (2).

A hearing-related medical history and noise exposure questionnaire was administered as an interview. History of noise exposure was determined by self-report. An individual was considered to have a positive history of occupational noise exposure if he/she reported holding a job that required

speaking in a raised voice or louder to be heard; being a farmer and driving a tractor without a cab; or having performed certain duties in the military: serving as a pilot or crew member on a plane, serving as a crew member on a tank, working in the engine room of a ship, or using grenades, mortars, shoulder-held grenade launchers or a weapons system requiring more than one person for operation. History of noisy leisure-time activities—including wood-working, metalworking, driving a noisy recreational vehicle, using power tools in yard work, using a chain saw, playing a musical instrument, and using firearms recreationally for hunting or target shooting—was also evaluated. However, leisure-time noise exposure did not significantly influence the association between NIDDM and hearing loss and was not included in the final model.

Data used in these analyses obtained as part of the BDES examination included blood pressure measured with a random zero sphygmomanometer following the Hypertension Detection and Follow-up Program protocol (28). Hypertension was defined as self-report of physician-diagnosed hypertension along with the use of antihypertensive medication or, in the absence of a positive self-report, by elevated systolic blood pressure  $>140$  mmHg or diastolic blood pressure  $>90$  mmHg at the time of the examination.

A medical history questionnaire that included questions regarding diabetes status and medication use was administered by interview. Nonfasting blood glucose was measured on venous blood using the hexokinase method. Serum glycosylated hemoglobin was determined using affinity chromatography (Isolab, Akron, OH), and serum creatinine was measured. A random urine sample was obtained and analyzed using an instrument for strip reading (Clinitek; Ames, Elkhart, IN). The presence of NIDDM was determined by self-report of physician-diagnosed diabetes at age 30 years or older along with the use of insulin, oral hypoglycemic agents, or diet to control glycemia or by self-report of diabetes with elevated blood glucose ( $>200$  mg/dl) or elevated glycosylated hemoglobin levels (age- and sex-specific cut points) (29). Additionally, individuals were classified as having diabetes if self-report of diabetes was negative but blood glucose or glycosylated hemoglobin levels were elevated at the time of the examination. Individuals with a self-report of diabetes who were not taking medication or following a diet to con-

trol glycemia and who had normal laboratory values were classified as having “questionable” diabetes.

Nephropathy was defined as present if there was a self-report of renal transplant or dialysis, if gross proteinuria ( $\geq 100$  mg/dl) was present, or if serum creatinine was elevated ( $>1.6$  mg/dl) at the time of the examination.

Stereoscopic 30° fundus photographs were graded for the presence of retinopathy in a masked fashion using the modified Airlie House classification scheme (29).

There were 83 (2.3%) individuals who participated in the EHLS but refused the 5-year follow-up examination of the BDES. For these participants, the medical history questions and blood pressure readings were obtained at the time of the hearing study examination. The average interval between the hearing and vision examinations was 4.5 days. About half (51%) were examined on the same day.

SAS (SAS Institute, Cary, NC, 1990) was used for all analyses. Multiple logistic regression was used to test the association between NIDDM and hearing loss while adjusting for possible confounders. Univariate analyses were used to identify potential confounders, which were then included in the models. Variables that did not act as confounders or effect modifiers were eliminated from subsequent models. Additionally, the association of duration of diabetes, glycemic control, and complications of diabetes with hearing loss were evaluated.

**RESULTS** — Of the 3,571 individuals who participated in the EHLS, 120 with missing interview data (diabetes diagnosis) and/or laboratory data were excluded. Ten individuals who reported a diabetes diagnosis prior to age 30 years were considered to have probable IDDM, and 68 participants who were classified as having “questionable” diabetes were excluded from analyses. Of the remaining 3,373 participants, 3,029 were classified as not having diabetes and 344 were classified as having NIDDM.

Descriptive characteristics comparing the group without diabetes to those with NIDDM are shown in Table 1. In general, participants with NIDDM were significantly older (69.6 vs. 65.1 years), were less educated, and had lower income levels than participants without diabetes. The group with NIDDM had a higher mean BMI (31.4 vs. 28.6 kg/m<sup>2</sup>), higher blood glucose levels (174.0 vs. 97.6 mg/dl), higher glycosylated hemoglobin values (9.7 vs. 6.0%), and

**Table 1—Descriptive characteristics of participants in the EHLS**

	Without diabetes	With diabetes	P value
n	3,029	344	
Age	65.1 ± 10.5	69.6 ± 9.5	0.0001
% Men	43.2	44.5	0.55
Education (%)			
<12 years	669 (22.1)	126 (36.6)	
12 years	1,408 (46.5)	133 (38.7)	
13–15 years	473 (15.6)	54 (15.7)	
≥16 years	477 (15.8)	31 (9.0)	<0.001
Income (\$)			
0–9,000	259 (9.3)	63 (20.7)	
10–19,000	649 (23.3)	87 (28.6)	
20–29,000	563 (20.2)	47 (18.8)	
30–44,000	629 (22.5)	48 (15.8)	
45–59,000	362 (13.0)	30 (9.9)	
60,000+	326 (11.7)	19 (6.3)	<0.001
BMI (kg/m <sup>2</sup> )	28.6 ± 5.2	31.4 ± 5.9	0.0001
GHb (%)	6.0 ± 0.7	9.7 ± 2.9	0.0001
Glucose (mg/dl)	97.6 ± 14.6	174.0 ± 84.9	0.0001
Cholesterol (mg/dl)	238.8 ± 44.7	235.7 ± 47.3	0.31
Smoking status (%)			
Never	1,390 (45.9)	173 (50.6)	
Past	1,176 (38.9)	144 (42.1)	
Current	460 (15.2)	25 (7.3)	0.01
Hypertension	1,425 (47.2)	256 (75.1)	<0.001
Occupational noise	1,663 (54.9)	204 (59.3)	0.07
Mean PTA (dB HL)	26.9 (+18.8)	33.3 (+20.5)	0.0001

Data for education, income, smoking status, hypertension, and occupational noise are given as n (%); data for age, BMI, GHb, glucose, and cholesterol are means ± SD.

lower HDL cholesterol levels (44.9 vs. 53.3 mg/dl); were more likely to have hypertension (75 vs. 47%); were less likely to be current smokers; and consumed less alcohol than participants without diabetes.

Univariate analysis revealed that the individuals with NIDDM were significantly more likely to have a hearing loss than were those without diabetes (hearing loss prevalence of 59 vs. 44%, *P* < 0.01). However, when controlling for age, the difference was not statistically significant (Fig. 1).

After controlling for age, sex, hypertension, education, history of occupational noise exposure, smoking status, and the interaction of hypertension with sex, the association between NIDDM and hearing loss (odds ratio [OR] 1.27, 95% CI = 0.97–1.67) was not statistically significant.

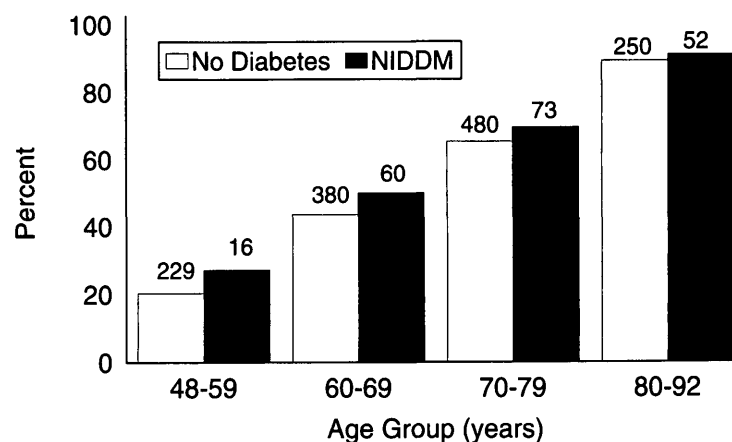
To address the issue of heterogeneity in the measure of hearing loss, subset analyses were conducted excluding individuals with hearing loss patterns that were not consistent with age-related hearing loss (*n* = 267). Excluded individuals reported a young age at onset of hearing loss (≤30 years),

reported a history of ear surgery, had a unilateral hearing loss, or had a conductive hearing loss (air-bone gap of ≥15 dB HL at 0.5 or 4 kHz) that, if treated and resolved, would leave them with normal hearing thresholds (PTA <25 dB HL based on bone

thresholds). There was a significant association between NIDDM and hearing loss (OR = 1.41, 95% CI = 1.05–1.88) (Table 2) when excluding these participants.

Glycated hemoglobin was not associated with hearing loss either when evaluating the entire cohort or when evaluating only those with NIDDM (Table 3). To investigate a possible threshold effect, glycated hemoglobin was modeled as a quadratic term and also divided into quartiles. The results of the multiple logistic regression models showed no association between glycemic control and hearing loss (data not shown). Additionally, there was no association between duration of diabetes (measured in years) and hearing loss (Table 3).

Because data from some of the earlier studies suggested an association between hearing loss and the presence of diabetic complications, the association of nephropathy and retinopathy with hearing loss was investigated. Because retinal microaneurysms are common, the relationship between moderate retinopathy (level 31 or greater in both eyes, *n* = 90) and hearing loss was assessed. Results of the multiple logistic regression models are shown in Table 4. There was no association between diabetic retinopathy and hearing loss. However, among individuals with NIDDM, those with nephropathy (*n* = 59) were significantly more likely to have a hearing loss than were those without nephropathy (*n* = 285; OR = 2.28, 95% CI = 1.04–5.00). As shown in Fig. 2, age-adjusted hearing thresholds were worse at every frequency for those with nephropathy compared with individuals without this complication. There was no difference by retinopathy status.



**Figure 1—Prevalence of hearing loss by diabetes status.**

**Table 2—Adjusted ORs of NIDDM and hearing loss**

	OR	95% CI	P value
Overall NIDDM	1.27	0.97–1.67	0.09
Subset NIDDM	1.41	1.05–1.88	0.02

ORs were calculated while controlling for age, sex, education, hypertension, hypertension/sex interaction, smoking status, and history of occupational noise. The subset NIDDM analysis excluded individuals with young age at onset of hearing loss ( $\leq 30$  years), unilateral hearing loss, history of ear surgery, and conductive loss.

**CONCLUSIONS** — This study demonstrated a modest association between NIDDM and hearing loss in the subset analysis that excluded participants with hearing loss inconsistent with presbycusis. This finding is consistent with some other reports in the literature (10–12,18) and suggests that individuals with diabetes may be more likely to have a hearing loss than other older adults. However, no association was found between diabetes and hearing loss overall; nor was there an association with glycemia.

The Framingham Heart Study found no association between diabetes or impaired glucose tolerance and hearing thresholds, but they did find a significant association between blood glucose and low-frequency hearing in women. In a re-analysis of our data, there was no significant association between NIDDM and low-frequency hearing loss (PTA of the thresholds at 250, 500, and 1,000  $>25$  dB HL) or high-frequency hearing loss (PTA of 4,000, 6,000, and 8,000 Hz  $>40$  dB HL).

The presence of diabetic nephropathy was significantly associated with hearing loss, but there was no association with retinopathy among those with NIDDM, which is consistent with some of the previous reports in the literature. Axelsson et al. (12) reported that hearing loss in people with diabetes was associated with nephropathy and severe

**Table 4—Adjusted ORs of complications of diabetes and hearing loss**

	OR	95% CI	P value
Retinopathy	0.94	0.52–1.68	0.83
Nephropathy	2.28	1.04–5.00	0.04

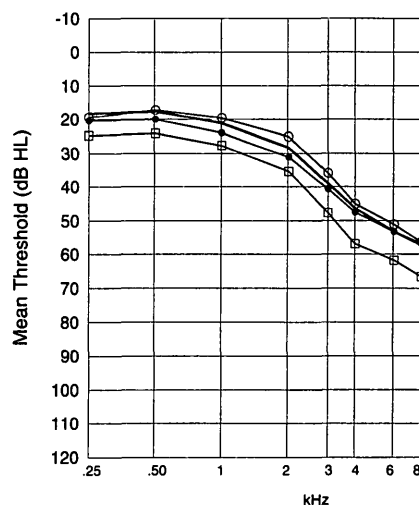
ORs were calculated while controlling for age, sex, education, hypertension, hypertension/sex interaction, smoking status, and history of occupational noise.

**Table 3—Adjusted ORs of duration, glycemic control, and hearing loss**

	OR	95% CI	P value
Within NIDDM			
Duration (1-year change)	0.99	0.96–1.02	0.58
Glycated hemoglobin (1% increase)	1.01	0.96–1.07	0.59
Entire population			
Glycated hemoglobin (1% increase)	1.01	0.92–1.10	0.89

ORs were calculated while controlling for age, sex, education, hypertension, hypertension/sex interaction, smoking status, and history of occupational noise.

retinopathy but not with less severe forms of retinopathy. In univariate analyses, Ferrer et al. (20) found microproteinuria and nephropathy to be significantly associated with hearing loss at 8 kHz and retinopathy to be significantly associated with hearing loss at 0.5–8 kHz. However, the individuals with retinopathy in Ferrer's study were older than those without retinopathy. No age-adjusted analyses were presented. In Beaver Dam, the prevalence of any retinopathy in those with NIDDM was 43.9%. However, a large percentage of these individuals had mild retinopathy consisting of microaneurysms only. To test the association of moderate retinopathy and hearing loss, only individuals with lesions more severe than microaneurysms in both eyes were evaluated ( $n = 90$ ). Only nine individuals had proliferative disease. The small numbers of people with severe retinopathy may have reduced our ability to see an association between retinopathy and hearing loss.

**Figure 2—Age- and sex-adjusted frequency thresholds by diabetes status and complications. —, no diabetes; —●—, NIDDM (no complications); —○—, retinopathy; —□—, nephropathy.**

Although the association between nephropathy and hearing loss was statistically significant, this may not reflect an association between microvascular complications of NIDDM and hearing loss. It is possible that nephrotoxic agents leading to nephropathy may also be ototoxic and contribute to hearing loss. In addition, treatment for nephropathy may have contributed to hearing loss. Longitudinal studies are necessary to better understand the association of microvascular complications of diabetes and hearing loss.

There was no association between duration of diabetes or glycemic control and hearing loss. Glycated hemoglobin measures control of diabetes over the preceding 2- to 3-month period. Although this gives a much better estimate of glycemic control than a single blood glucose measure, it still measures control over a very short time period. The cross-sectional nature of this study may explain the lack of association between glycated hemoglobin and hearing loss. In most cases, hearing loss is a gradual process developing over several years, so it is unlikely that a single glycated hemoglobin measure concurrent with the hearing evaluation would be associated with hearing loss.

In summary, these data suggest a weak association between NIDDM and hearing loss. Although this is the largest study to date to address the association of diabetes and hearing loss, the cross-sectional nature of these analyses does not allow the establishment of temporal order between NIDDM and hearing loss; some of the participants may have had a hearing loss before the onset of diabetes. Longitudinal studies are necessary to confirm an association between NIDDM and risk of hearing loss and to evaluate the effects of glycemic control and microvascular complications.

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