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Association of Iron Deficiency Anemia With Hearing Loss in US Adults

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IMPORTANCE Hearing loss in the US adult population is linked to hospitalization, poorer self-reported health, hypertension, diabetes, and tobacco use. Because iron deficiency anemia (IDA) is a common and easily correctable condition, further understanding of the association between IDA and all types of hearing loss in a population of US adults may help to open new possibilities for early identification and appropriate treatment.

OBJECTIVE To evaluate the association between sensorineural hearing loss (SNHL) and conductive hearing loss and IDA in adults aged 21 to 90 years in the United States.

DESIGN, SETTING, AND PARTICIPANTS The prevalence of IDA and hearing loss (*International Classification of Diseases, Ninth Revision* codes 389.1 [SNHL], 389.0 [conductive hearing loss], and 389 [combined hearing loss]) was identified in this retrospective cohort study at the Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania. Iron deficiency anemia was determined by low hemoglobin and ferritin levels for age and sex in 305 339 adults aged 21 to 90 years. Associations between hearing loss and IDA were evaluated using χ^2 testing, and logistic regression was used to model the risk of hearing loss among those with IDA. The study was conducted from January 1, 2011, to October 1, 2015.

MAIN OUTCOMES AND MEASURES Hearing loss.

RESULTS Of 305 339 patients in the study population, 132 551 were men (43.4%); mean (SD) age was 50.1 (18.5) years. There was a 1.6% (n = 4807) prevalence of combined hearing loss and 0.7% (n = 2274) prevalence of IDA. Both SNHL (present in 26 of 2274 individuals [1.1%] with IDA; $P = .005$) and combined hearing loss (present in 77 [3.4%]; $P < .001$) were significantly associated with IDA. Logistic regression analysis confirmed increased odds of SNHL (adjusted odds ratio [OR], 1.82; 95% CI, 1.18-2.66) and combined hearing loss (adjusted OR, 2.41; 95% CI, 1.90-3.01) among adults with IDA, after adjusting for sex.

CONCLUSIONS AND RELEVANCE Iron deficiency anemia was associated with SNHL and combined hearing loss in a population of adult patients. Further research is needed to better understand the potential links between IDA and hearing loss and whether screening and treatment of IDA in adults could have clinical implications in patients with hearing loss.

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Supplemental content

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In 2014, approximately 15% of adults reported difficulty with hearing, with the highest prevalence among white men.[1] Hearing loss increases with each decade of life, affecting 40% to 66% of adults older than 65 years and 80% of those older than 85 years.[2,3] Risk factors for earlier onset of adult hearing loss include hypertension, diabetes, and tobacco use.[3,4] Sudden sensorineural hearing loss (SNHL) is characterized by a rapid deterioration in hearing function that occurs in less than a 72-hour period. The mechanism is unknown, but a recent study by Chung et al[5] found a significant association between iron deficiency anemia (IDA) and sudden SNHL (odds ratio [OR], 1.34; 95% CI, 1.11-1.61; $P < .01$), which was most prominent in patients younger than 60 years. Iron deficiency anemia is a subset of anemia in which patients exhibit low hemoglobin, serum ferritin, and serum iron levels and increased soluble transferrin receptor levels. In US adults, IDA is usually a result of blood loss and often responds well to reversal of the source of blood loss and oral iron supplementation.[6]

Although the role of iron in the inner ear has not been clearly established, blood supply to this area is highly sensitive to ischemic damage. Sudden SNHL may have a vascular cause potentially exacerbated by IDA as described in a rat model of iron deficiency and sudden SNHL. This study identified defects in the cochlea, including strial atrophy[7] and reduced spiral ganglion cells, with effects on the stereocilia of the inner and outer hair cells.[7,8] The role of iron in the vasculature and nervous system raises the possibility of its association with other common types of adult hearing loss beyond sudden SNHL. Because IDA is a common and reversible condition, further understanding of the association between IDA and all types of hearing loss in a population of US adults may open new possibilities for treatment. Thus, the objective of this study was to examine the association between IDA and SNHL, conductive hearing loss (CHL), and combined hearing loss among a cohort of adult patients aged 21 to 90 years. Based on previous reports[5] of sudden SNHL and the mechanical component involved in CHL, the hypothesis was that IDA would demonstrate a stronger association with SNHL compared with CHL.

Key Points

Question Is iron deficiency anemia associated with hearing loss in the adult population?

Findings In this retrospective cohort study of 305 339 young to elderly adults, iron deficiency anemia was positively associated with sensorineural hearing loss and the presence of combined hearing loss.

Meaning Additional studies to examine how iron supplementation influences hearing status are warranted.

Methods

Study Population

We performed a retrospective cohort study using data obtained from deidentified electronic medical records from the Penn State Milton S. Hershey Medical Center in Hershey, Pennsylvania. Data were extracted using the National Institutes of Health–supported Informatics for Integrating Biology and the Bedside electronic medical records query tool.[9,10] Patients were included if they were aged 21 to 90 years with at least 1 outpatient, inpatient, or emergency department visit between January 1, 2011, and October 1, 2015. Patients with sickle cell disease (identified as at least 1 *International Classification of Diseases, Ninth Revision* [*ICD-9*] code for 282.6) were excluded owing to previous studies linking sickle cell anemia with hearing loss.[11-17] The study was determined to be exempt by the Pennsylvania State University College of Medicine Institutional Review Board, which also waived the need for patient informed consent because deidentified data were used.

Individuals with IDA were identified based on the presence of at least 1 low serum ferritin (<12.0 ng/mL) value (to convert to picomoles per liter, multiply by 2.247) and 1 low serum hemoglobin value between January 1, 2011, and October 1, 2015. Low hemoglobin values were defined in a previous National Health and Nutritional Examination Survey (NHANES) III study by an expert panel (men: 21-49 years, <13.7 g/dL; 50-69 years, <13.3 g/dL; and ≥70 years, <12.4 g/dL; women: 21-69 years, <12.0 g/dL; ≥70 years, <11.8 g/dL [to convert to grams per liter, multiply by 10]).[18]

Patients were identified as having hearing loss if they had at least 1 encounter associated with 1 of the following spectra of *ICD-9* codes: 389.0 (CHL), 389.1 (SNHL), or 389 (combined hearing loss). Patients meeting these criteria for hearing loss were categorized as having CHL, SNHL, or combined hearing loss. Combined hearing loss was defined as any combination of CHL, SNHL, deafness, and unspecified hearing loss. Covariates included age (21-69 and ≥70 years) and sex (male and female). Hearing loss–related *ICD-9* codes may have been added by a primary care physician, otolaryngologist, or audiologist following a visit with a hearing-related symptom. Formal audiogram testing would not be required for a clinician to select 1 of these codes.

Statistical Analysis

Prevalence of IDA and hearing loss are reported. Two-sided χ^2 testing was performed and ORs were determined via 2 × 2 contingency tables. In addition, multivariate conditional logistic regression analysis (adjusted for sex) was performed to obtain adjusted ORs and 95% CIs. All statistical testing was performed using R, version 3.2.3 software (The R Project for Statistical Computing).

Results

Demographics

Overall, a total of 305 339 individuals aged 21 to 90 years were identified in the study population. Of these, 132 551 were men (43.4%); mean (SD) age was 50.1 (18.5) years. This cohort was identified as having at least 1 outpatient, inpatient, or emergency department visit at Penn State Hershey Medical Center from 2011 to 2015. The prevalence of IDA was 0.7% (n = 2274). Consistent with published data,[19] IDA was more prevalent in

Table 1. Demographics of 305 339 Patients Included in Analysis

Characteristic	Total, No.	No HL, No. (%)	Combined HL		Sensorineural HL		Conductive HL	
			No. (%)	*P* Value[a]	No. (%)	*P* Value[a]	No. (%)	*P* Value[a]
Total, No.	305 339	300 532 (98.4)	4807 (1.6)	NA	2019 (0.7)	NA	492 (0.2)	NA
Age, y								
21-69	252 228	248 902 (98.7)	3326 (1.3)	<.001	1309 (0.5)	<.001	396 (0.2)	.19
70-90	53 111	51 630 (97.2)	1481 (2.8)		708 (1.3)		96 (0.2)	
Sex								
Male	132 551	130 240 (98.3)	2311 (1.7)	<.001	1000 (0.7)	<.001	234 (0.2)	.07
Female	172 788	170 289 (98.6)	2499 (1.4)		1017 (0.6)		258 (0.1)	
IDA								
Yes	2274	2197 (96.6)	77 (3.4)	<.001	26 (1.1)	.005	5 (0.2)	.63
No	303 065	298 335 (98.4)	4730 (1.6)		1993 (0.7)		487 (0.2)	

Abbreviations: HL, hearing loss; IDA, iron deficiency anemia; NA, not applicable.

[a] *P* values were calculated by 2-tailed χ^2 test for each HL group compared with the no HL group.

Table 2. Logistic Regression to Assess the Association Between Iron Deficiency Anemia and Hearing Loss[a]

Characteristic	Adjusted OR (95% CI)		
	Sensorineural HL	Conductive HL	Combined HL
Iron deficiency anemia[b]	1.82 (1.18-2.66)	1.51 (0.54-3.28)	2.41 (1.90-3.01)
Age	1.04 (1.03-1.04)	1.00 (0.99-1.01)	1.03 (1.02-1.03)
Sex	1.28 (1.18-1.40)	1.18 (0.99-1.41)	1.21 (1.14-1.28)

Abbreviations: HL, hearing loss; OR, odds ratio.

[a] Iron deficiency anemia was defined by serum ferritin levels less than 12 ng/mL (to convert to picomoles per liter, multiply by 2.247) and hemoglobin levels based on sex and age (men: 21-49 years, <13.7 g/dL; 50-69 years, <13.3 g/dL; and ≥70 years, <12.4 g/dL; women: 21-69 years, <12.0 g/dL; ≥70 years, <11.8 g/dL (to convert to grams per liter, multiply by 10).

[b] Analysis was adjusted for sex.

women compared with men (prevalence, 1.1% vs 0.3%; $P < .001$). The prevalence of combined hearing loss was 1.6% (n = 4807), and SNHL (0.7%) was more prevalent than CHL (0.2%). Iron deficiency anemia was positively associated with both SNHL (1.1%; $P = .005$) and the presence of combined hearing loss (3.4%; $P < .001$) (**Table 1**).

Association of IDA and Hearing Loss

After adjustment for sex, IDA remained associated with an increased odds of combined hearing loss (adjusted OR, 2.41; 95% CI, 1.90-3.01). Similarly, IDA was associated with increased odds of SNHL (adjusted OR, 1.82; 95% CI, 1.18-2.66) in the adjusted analysis (**Table 2**). Serum ferritin and hemoglobin are not usually tested unless the diagnosis warrants it; to account for this potential underrepresentation of individuals with IDA, a sensitivity analysis was performed using an IDA prevalence of 3% for women and 1% for men. Overall, similar results were seen, indicating increased odds of both SNHL and combined hearing loss with IDA (eTable in the Supplement).

Discussion

Our study demonstrates increased odds of hearing loss among adults aged 21 to 90 years with IDA. These findings are consistent with those of another observational study in Taiwan that identified an association between IDA and sudden SNHL most prominently in individuals younger than 60 years.[5] Previous studies[7,8,20-26] suggest several potential mechanisms by which IDA may affect hearing health; however, it is unknown whether early diagnosis and treatment of IDA could positively affect the overall health status of adults with hearing loss.

The cochlea is highly susceptible to ischemic damage since only the labyrinthine artery supplies blood to this area.[27] Iron deficiency anemia has been demonstrated to be a potential risk factor for ischemic stroke due to lower hemoglobin levels leading to impaired oxygen-carrying capacity.[20,21] Individuals with vascular disease have been shown to have a higher risk for developing sudden SNHL.[5,28-32] Another potential vascular mechanism linking IDA and hearing loss is the increased risk of IDA in patients with reactive thrombocytosis.[22,23] Iron is a regulator of thrombopoiesis, and previous associations between blood loss and thrombocytosis have been established.[33,34] This hypothesis is further substantiated by a case report that demonstrated acute SNHL in a patient with marked thrombocytosis that was reversed after plasmapheresis.[35] Iron deficiency results in the degradation of lipid saturase and desaturase, impairing energy production and, consequently, myelin production.[24] Damage to the myelin surrounding the auditory nerve impairs conduction velocity resulting in noise-induced hearing loss,[25] possibly due to changes in sodium channel density.[26]

The present study found an association between IDA and hearing loss. Iron deficiency anemia is easily treated with several months of oral iron supplementation.[6] A study using the NHANES data from 1999-2002 found that individuals with

healthier dietary habits were able to detect higher-frequency noises.[36] Treatment of IDA will naturally improve anemia and replenish iron stores. Iron deficiency anemia is associated with a large number of related morbidities (eg, fatigue and reduced work capacity), which are also likely to improve with treatment.[37-56] Additional studies are needed to determine whether there is a link between iron supplementation and hearing status.

Limitations

There are limitations to this analysis that should be considered. The use of laboratory results (ie, serum ferritin and hemoglobin levels) increased the specificity of the IDA definition in our study but reduced the sensitivity. With the wide availability of laboratories not affiliated with our institution and with Informatics for Integrating Biology and the Bedside unable to include data that are not internal, the prevalence of IDA and hearing loss in this study may be falsely reduced. A sensitivity analysis was performed to address this limitation. Using an IDA prevalence of 1% for men and 3% for women, the same analyses were performed. The data remained significant, indicating that although the sensitivity of the analysis is reduced by the present methods, the positive association between IDA and hearing loss remains (eTable in the Supplement). In addition, identifying whether iron deficiency or anemia alone is associated with hearing loss is unable to be accurately performed with this analysis since hemoglobin and serum ferritin are not often tested in the general population. Therefore, distinguishing between iron deficiency, anemia, and IDA would not be definitive.

The prevalence of combined hearing loss, SNHL, and CHL was also lower than has been reported in the literature.[3] An analysis using NHANES data from 2001 to 2008 reported a prevalence of 3.2% (95% CI, 1.4%-5.1%) of bilateral and unilateral hearing loss of more than 25 dB among individuals aged 20 to 29 years, increasing with each decade of life with a prevalence of 89.1% (95% CI, 86.1%-92.0%) for those 80 years or older. In contrast, this present investigation was an observational study of health care–seeking adults, and the results may not be generalizable to the rest of the US population.[57] Patients with hearing loss in this analysis were defined by *ICD-9* codes; thus, there are no diagnostic values for comparison. There were likely instances in which hearing loss was not consistently coded due to human error during data entry, neglect to include the *ICD-9* code for hearing loss in the patients' medical records, or exclusion from the query due to billing before January 2011. Similarly, adjusting for potential risk factors, such as smoking status, is unable to be performed in Informatics for Integrating Biology and the Bedside owing to noninclusion in the database. Adjusting for other potential risk factors, such as diabetes and hypertension, is possible with our model, but the results would then be uninterpretable because of the high collinearity between age and these confounding comorbidities.

Conclusions

An association exists between IDA in adults and hearing loss. The next steps are to better understand this correlation and whether promptly diagnosing and treating IDA may positively affect the overall health status of adults with hearing loss.

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Study concept and design: Schieffer, Connor, Pawelczyk, Sekhar.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Schieffer, Sekhar.
Critical revision of the manuscript for important intellectual content: All authors.
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