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Iron Deficiency Anemia is Associated with Hearing Loss in the Adult Population

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Abstract

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

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

DESIGN—The prevalence of IDA and hearing loss (ICD-9 codes 389.1 (SNHL), 389.0 (conductive hearing loss), and 389 (combined hearing loss)) were identified in this retrospective cohort study. IDA was determined by low hemoglobin and ferritin levels for age and sex. Associations between hearing loss and IDA were evaluated using Chi squared test. Logistic regression modeled the risk of hearing loss among those with IDA.

SETTING—Penn State Health Milton S. Hershey Medical Center, Hershey, PA.

PARTICIPANTS—Adults 21–90 years of age.

MAIN OUTCOME MEASURES—Hearing loss

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RESULTS—Out of 305,339 patients in the study population, there was a 1.6% (n=4,807) prevalence of hearing loss and 0.8% (n=2,274) prevalence of IDA. Both SNHL and presence of combined hearing loss was significantly associated with IDA. Logistic regression confirmed increased odds of SNHL (adjusted 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—IDA 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.

In 2014, about 15% of adults reported difficulty hearing, with the highest prevalence among white men.¹ Hearing loss increases with each decade of life, affecting 40–66% of adults older than 65 years-old 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 etiology is unknown, but a recent study by Chung *et al.* found a significant association between iron deficiency anemia (IDA) and sudden SNHL [OR: 1.34 (95% CI: 1.11–1.61), p<0.01], which was most prominent in patients under 60 years-old.⁵ IDA is a subset of anemia in which patients exhibit low hemoglobin, serum ferritin, serum iron, and increased soluble transferrin receptor. In United States adults, IDA is usually a result of blood loss, and usually responds well to reversal of the source of blood loss and oral iron supplementation.⁶

While the role of iron on 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 etiology potentially exacerbated by IDA as described in a rat model of iron deficiency and sudden SNHL. This study identified defects in the cochlea, including stria atrophy⁷ 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. As IDA is a common and reversible condition, further understanding the association between IDA and all types of hearing loss in a population of United States 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 all hearing loss among a cohort of adult patients 21–90 years-old. Based on previous reports with sudden SNHL and the mechanical component involved in CHL, the hypothesis was that IDA would demonstrate a stronger association with SNHL compared to CHL.

Methods

Study Population

This study was a retrospective cohort study using data obtained from de-identified electronic medical records from the Penn State Milton S. Hershey Medical Center in Hershey, PA. The study was determined to be exempt by the Pennsylvania State University College of Medicine Institutional Review Board. Data was extracted using the National Institutes of

Health-supported Informatics for Integrating Biology and the Bedside (i2b2) electronic medical records query tool^{9,10}. Patients were included if they were 21–90 years of age with at least one outpatient, inpatient, or emergency department visit between January 1, 2011 and October 1, 2015. Patients with sickle cell disease (identified as at least one ICD-9 code for 282.6) were excluded due to previous studies linking sickle cell anemia with hearing loss.^{11–17}

Individuals with IDA were identified based on the presence of at least one low serum ferritin (<12.0 ng/dl) value and one 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 : males ages 21–49 years-old <13.7 g/dl, males ages 50–69 years-old <13.3 g/dl, males 70 years-old <12.4 g/dl, females ages 21–69 years old <12.0 g/dl, females 70 years-old <11.8 g/dl.¹⁸

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

Statistical Analysis

Prevalence of IDA and hearing loss are reported. Chi squared test (two-sided) and odds ratios were performed via 2x2 contingency tables. Additionally, multivariate conditional logistic regression analysis (adjusted for sex) were performed to obtain adjusted odds ratios and 95% confidence intervals. All statistics were performed using R software (The R Project for Statistical Computing, Vienna, Austria).

Results

Demographics

Overall, a total of 305,339 individuals 21–90 years of age were identified in the study population. This cohort of subjects was identified as having at least one outpatient, inpatient, or emergency department visit at Penn State Hershey Medical Center from 2011–2016. The prevalence of IDA was 0.8% (n=2,274). Consistent with published data¹⁹, IDA was more prevalent in females (prevalence: 1.1%) compared to males (prevalence: 0.3%, $p < 0.001$). The prevalence of combined hearing loss was 1.6% (n=4,807) and SNHL (0.7%) was more prevalent than CHL (0.2%). IDA was positively associated with both SNHL ($p=0.005$) and presence of combined hearing loss ($p < 0.0001$) (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 also 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 commonly 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 females and 1% for males. Overall, similar results were seen indicating increased odds of both SNHL and combined hearing loss with IDA (data not shown).

Discussion

Our study demonstrates increased odds of hearing loss among adults ages 21–90 with IDA. These findings are consistent with another observational study in Taiwan that identified an association between IDA and sudden SNHL most prominently in individuals under 60 years-old.⁵ Recent studies suggest several potential mechanisms by which IDA may affect hearing health; however, it is unknown whether early diagnosis and treatment of IDA could positively impact 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.²⁰ IDA has been demonstrated to be a potential risk factor for ischemic stroke due to lower hemoglobin levels leading to impaired oxygen carrying capacity.^{21,22} Individuals with vascular disease have been shown to have higher risk for developing sudden SNHL.^{5,23–27} Another potential vascular mechanism linking IDA and hearing loss is the increased risk of IDA patients for reactive thrombocytosis.^{28,29} Iron is a regulator of thrombopoiesis and previous associations between blood loss and thrombocytosis have been established.^{30,31} This hypothesis is further substantiated by a case report which demonstrated acute SNHL in a patient with marked thrombocytosis reversed following plasmapheresis.³² Iron deficiency results in the degradation of lipid saturase and desaturase, impairing energy production, and consequently, myelin production.³³ Damage to the myelin surrounding the auditory nerve impairs conduction velocity resulting in noise-induced hearing loss³⁴, possibly due changes to sodium channel density.³⁵

This study found an association between IDA and hearing loss. IDA is easily treated with several months of oral iron supplementation.⁶ A study using the NHANES data from 1999–2002 found that those with healthier dietary habits were able to detect higher frequency noises.³⁶ Treatment of IDA will naturally improve anemia and replenish iron stores. IDA is associated with a large number of related morbidities (fatigue, 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.

There are limitations to this analysis which should be considered. The use of laboratory results (i.e., serum ferritin and hemoglobin) increased the specificity of the IDA definition our study but reduced the sensitivity. With the wide availability of laboratories not affiliated with this institution and with i2b2 unable to include data that is 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 males and 3% for females, the same analyses were performed. The data remained significant, indicating that although the sensitivity of the analysis is reduced by the current analysis methods, the positive association between IDA and HL still remains (data not shown). Additionally, 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 commonly tested in the general population. Therefore, distinguishing between iron deficiency, anemia, and IDA would not be definitive.

The prevalence of hearing loss, SNHL and CHL were also lower than has been reported in the literature.³ An analysis using NHANES data from 2001–2008 reported a prevalence of 3.2% (95% CI: 1.4–5.1%) of bilateral and unilateral hearing loss >25 dB among 20–29 year-olds, increasing with each decade of life with a prevalence of 89.1% (95% CI: 86.1–92.0) for those 80 years old. In contrast, this was an observational study of health care seeking adults; and the results may not be generalizable to the rest of the population.⁵⁷ Patients with hearing loss in this analysis were defined by ICD-9 code, 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, neglecting to include the ICD-9 code for hearing loss in the patients' chart, or exclusion from the query due to billing prior to January 2011. Similarly, adjusting for potential risk factors, such as smoking status, is unable to be performed in i2b2 due to non-inclusion in the database. Adjusting for other potential risk factors, such as diabetes and hypertension is possible with our model but the results would be uninterpretable due to the high collinearity between age and these confounding comorbidities.

Conclusions

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

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Demographics (n=305,339)

Characteristics	Total n	No HL n (%)	Combined HL n (%)	Combined HL p-value	SNHL n (%)	SNHL p-value	CHL n (%)	CHL p-value
Total n	305,339	300,532 (98.4%)	4,807 (1.6%)		2,019 (0.7%)		492 (0.2%)	
Age								
21-69	252,228	248,902 (98.7%)	3,326 (1.3%)	<0.001	1,309 (0.5%)	<0.001	396 (0.2%)	0.190
70-90	53,111	51,630 (97.2%)	1,481 (2.8%)		708 (1.3%)		96 (0.2%)	
Sex								
Males	132,551	130,240 (98.2%)	2,311 (1.7%)	<0.001	1,000 (0.7%)	<0.001	234 (0.2%)	0.065
Females	172,788	170,289 (98.6%)	2,499 (1.4%)		1,017 (0.6%)		258 (0.1%)	
Iron Deficiency Anemia Status								
IDA	2,274	2,197 (96.6%)	77 (3.4%)	<0.001	26 (1.1%)	0.005	5 (0.2%)	0.633
No IDA	303,065	298,335 (98.4%)	4,730 (1.6%)		1,993 (0.7%)		487 (0.2%)	

P value calculated by two-tailed chi squared test for each hearing loss group compared to the no hearing loss group.

HL, hearing loss; SNHL, sensorineural hearing loss; CHL, conductive hearing loss; IDA, iron deficiency anemia

Table 2

Logistic regression to assess the association between iron deficiency anemia¹ and hearing loss

	Sensorineural Hearing Loss	Conductive Hearing Loss	Any Hearing Loss
Iron Deficiency Anemia ²	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)

¹Iron deficiency anemia defined by serum ferritin <12 ng/ml and hemoglobin based on gender and age: males ages 21–49 years-old <13.7 g/dl; males ages 50–69 years-old <13.3 g/dl; males 70 years-old <12.4 g/dl; females ages 21–69 years-old <12.0 g/dl; females 70 years-old <11.8 g/dl

²Analysis was adjusted for sex

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