Lipids in Health and Disease

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Lipid metabolism and hearing loss: association of non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) with adolescent hearing health

Zhe Peng[1,2*], Qian Wu[1,2], Chun-li Zhao[1,2] and Shu-sheng Gong[1,2*]

Abstract

Background The ratio of non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol (NHHR) is a novel lipid measure for assessing the risk of cardiovascular disease. Lipid metabolism disorders are reportedly associated with hearing impairment. This study aimed to investigate the potential association between NHHR and hearing.

Methods The data used in this study were obtained from the National Health and Nutrition Examination Survey (NHANES) cycles of 2005–2010 and 2017–2018, including 4,296 participants aged 6–19 years. The NHHR was calculated from lipid profiles, and hearing was assessed using pure-tone audiometry. Weighted multivariate logistic regression analyses were used to investigate the association between the NHHR and hearing loss. Subgroup and sensitivity analyses were performed to verify the robustness of the results.

Results Univariate analysis revealed significant associations between the NHHR and hearing threshold at all categorized frequency (low, speech, or high-frequency) ($P < 0.001$). Three models were used: an unadjusted model, a model adjusted for age, sex, and race, and a model further adjusted for PIR, BMI, and diabetes. Multiple regression analysis confirmed these associations consistently across all models. When considered as a continuous variable, NHHR had a significant association with enhanced hearing thresholds at all categorized frequencies: low-frequency (β:0.56, 95% CI: 0.36–0.75), speech-frequency (β:0.55, 95% CI: 0.36–0.7), and high-frequency (β:0.55, 95% CI: 0.36–0.74). The adjusted models showed persistent positive correlations after controlling for covariates. The NHHR was consistently positively associated with hearing loss. The NHHR and auditory thresholds showed a general dose-response association across all frequencies.

*Correspondence:
Zhe Peng
tsulinhjm@gmail.com
Shu-sheng Gong
gongss1962@163.com

Full list of author information is available at the end of the article

Conclusions NHHR is a promising biomarker for predicting adolescent hearing threshold shifts and hearing loss. The study highlights the importance of early lipid monitoring and management as strategies to prevent or reduce hearing impairment.

Keywords NHHR, Hearing, NHANES, Children, Adolescents, Cross-sectional study

Background

Hearing loss (HL) affects millions in the United States of America (USA), with 12.5% of children aged 6–19, based on NHANES data (HL is defined as a pure-tone audiometry > 15 dB in one ear. Its prevalence among adolescents aged 12–19 has increased over the past decade, making it a growing public health concern [1]. Sensorineural hearing loss (SNHL) has significant medical, social, and cultural impacts [2]. Individuals from families staying under the federal poverty line are more likely to have HL than those living above the federal poverty line. Some patients are likely to have mild congenital HL that is not detected until early childhood. Surveys have shown that more youths have measured HL than self-reporting indicates, suggesting that self-report screenings may miss mild HL cases [3]. Current perspectives focus on mild HL, which affects 10–15% of pupils, school performance, and social interactions [4, 5]. Strong evidence shows that HL > 40 dB negatively affects classroom learning and vocational achievement [3].

Although HL has various causes, the hypothesis that inner ear microcirculatory disorders contribute to it remains debated and challenging. Atherosclerosis, diabetes, lipid disorders, and hypertension have recently been associated with cardiovascular degeneration [6–8]. Hyperlipidemia reduces blood vessel elasticity and induces atherosclerosis, leading to microangiopathy. The susceptibility of the cochlea to hemodynamics can be attributed to its anatomy. The cochlea, relying on a single artery supply and having few collateral arteries, is weak and very sensitive to vascular alterations [9, 10]. Hyperglycemia, combined with hyperlipidemia and atherosclerosis, can worsen HL in apolipoprotein E knockout (ApoE-KO) mice by accelerating cell apoptosis [11]. Animal experiments have shown that dyslipidemia can cause sudden sensorineural hearing loss (SSNHL), affecting the blood supply to the cochlea [12]. Statistical data from various populations have also confirmed that dyslipidemia can serve as a predictive factor for SSNHL [8, 13]. Dyslipidemia, which is characterized by abnormal blood lipid levels, is associated with various vascular disorders that can affect hearing. Studies have shown that individuals with elevated cholesterol and triglyceride levels may have a higher risk of HL owing to compromised blood flow to the auditory system [14, 15]. For example, specific studies have found a significant correlation between hyperlipidemia and an increased incidence of SSNHL [8, 16, 17], suggesting that lipid imbalances can contribute to inner ear damage.

Therefore, potential indicators of lipid metabolism may be important in identifying early-stage HL risk and facilitating timely intervention, although further research is needed to confirm their role. Various lipid indicators including low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol have been investigated for their potential link to HL. Compared to traditional lipid markers, the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) offers a more comprehensive reflection of an individual's lipid metabolism status [18–20]. In adult populations, the NHHR is closely associated with the occurrence of cardiovascular events and can effectively predict the risk of atherosclerotic cardiovascular disease [21]. However, the application and research of the NHHR in children and adolescents, a key demographic, remains relatively understudied.

Childhood and adolescence are periods of rapid physical growth and development, critical for preventing future cardiovascular diseases. During this phase, lipid levels affect short-term health and have far-reaching implications for cardiovascular health in adulthood. Studies have shown that lipid abnormalities in childhood can persist into adulthood, increasing the risk of cardiovascular diseases [22]. Therefore, early identification and intervention for lipid metabolism abnormalities in this population are particularly important.

Most existing studies have focused on the relationship between the NHHR and cardiovascular health in adults, with relatively few studies on children and adolescents. This knowledge gap limits the ability to utilize NHHR for risk assessment and early intervention in this population. Additionally, with the rising prevalence of obesity and metabolic syndrome in children, exploring the predictive value of the NHHR in this group is becoming increasingly urgent. This study addresses this gap by investigating the role of NHHR in hearing impairment. This unique lipoprotein ratio accounts for both HDL-C and non-HDL-C, minimizing the restrictions of previous lipid-only research [18, 23]. The NHHR includes all atherogenic lipoproteins, potentially linked more closely to HL pathophysiology than HDL-C or LDL-C levels alone. It was hypothesized that the NHHR could serve as a sensitive and comprehensive biomarker for identifying the potential impact of lipid metabolism abnormalities on children's health. This research aims to provide scientific

evidence for the establishment of new screening standards and early intervention strategies to improve long-term health outcomes in children. This will aid the development of more effective public health strategies to improve the health of children and adolescents.

NHANES data from 2005–2006,2007–2008,2009–2010 and 2017–2018 were used for this cross-sectional investigation. These statistics include complete nutritional and health information, including detailed audiometric measurements and lipid profiles, thus forming a robust foundation for analysis.

Methods

This study used the data from the National Health and Nutrition Examination Survey (NHANES) data. The current analysis used data from the 2005–2006, 2007–2008, 2009–2010, and 2017–2018 survey cycles, including socioeconomic, demographic, nutritional, and health-related information. The study protocol was approved by the Research Ethics Review Board of the National Health and Nutrition Examination Survey.

Study population

The analysis included subjects from the four NHANES cycles spanning 2005–2010 and 2017–2018, focusing exclusively on children and adolescents aged 6 to 19 years. Additional exclusion criteria were as follows: (1) missing complete NHHR data. (2) missing complete audiometric data. (3) ear examinations were not eligible for inclusion, for example, ear tubes, infected cases, abnormal otoscopic findings, cerumen blockage, or substandard tympanometry. (4) lack of completed essential covariates such as Body Mass Index (BMI), Poverty Income Ratio (PIR), and diabetes. A total of 40,228 participants were initially enrolled; after exclusion, 4,296 eligible individuals were included in the final analysis. (Fig. 1).

NHHR assessment

The primary independent variable of the study was NHHR, which was determined from lipid levels measured using Roche Cobas 6000 and Modular P analyzers through enzymatic methods. NHHR was calculated as non-HDL-C (Total Cholesterol minus HDL-C) divided by the HDL-C level.

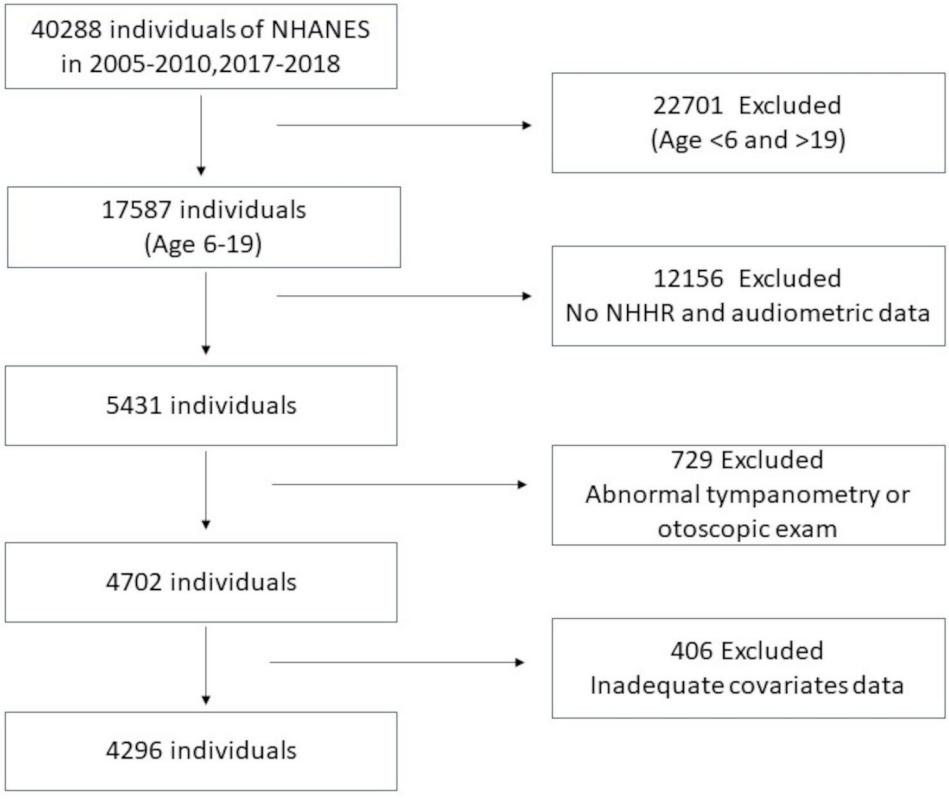

Fig. 1 Selection procedure for study participants. This figure illustrates the participant selection process from the National Health and Nutrition Examination Survey (NHANES) data spanning 2005–2010 and 2017–2018. Adolescents aged 6–19 years were initially considered. Exclusions were applied for incomplete data on hearing assessments, otoscopic examinations, tympanograms, or NHHR. Additional exclusions were made for abnormal otoscopic findings, poor-quality tympanogram results, or tympanograms showing a compliance of ≤ 0.3 mL. The final study cohort comprised 4,296 adolescents

Hearing assessment

This study assessed the association between NHHR and hearing in American adolescents, using both categorical (binary yes/no HL) and continuous (pure-tone audiometry, PTA) statistical approaches. In an acoustically controlled setting, experienced audiologists performed PTA to assess hearing. Testing covered frequencies from 0.5 to 8 kHz, with duplicate tests at 1 kHz to ensure reliability. HL was defined as the PTA greater than or equal to 20 dB within each categorized frequency range (low-, speech-, or high-frequency), following the recommendations of the World Health Organization (2021) [24]. HL was further categorized as low-frequency HL, speech-frequency HL, and high-frequency HL. The results were categorized into low-frequency (0.5, 1, 2 kHz) [15, 25, 26], speech-frequency (0.5, 1, 2, 4 kHz) [26–28], and high-frequency (4, 6, 8 kHz) hearing thresholds [15, 26]. For each category, the hearing thresholds were averaged across the specified frequencies to provide an overall threshold for low-, speech-, and high-frequency hearing loss.

Covariates

Potential covariates that could confound the relationship between the NHHR and auditory threshold were accounted for in the multivariate-adjusted model. The covariates included age, sex, race, PIR, BMI, and diabetes status.

Demographic details including age, sex, race, PIR, and diabetes status were obtained using a standardized questionnaire. Physical examinations were used to obtain BMI data, which was divided into three categories: normal weight (<25 kg/m²), overweight (≥25 kg/m² and ≤30 kg/m²), and obese (≥30 kg/m²) [29]. Household income levels were determined using the self-reported family PIR, which was divided into tertiles for subgroup analysis. Diabetes was defined as either a self-reported medical diagnosis or the use of antihyperglycemic medications. Participants who answered 'yes' or 'borderline' to either question were classified as having diabetes [15, 30].

Statistical analysis

Data from the 2005–2010 and 2017–2018 NHANES cycles were combined, and 8-year sampling weights were created using the 2-year sampling weights (WTMEC2YR) provided by the NHANES. These weights account for oversampling, survey non-response, and post-stratification inherent in the complex survey design. All the analyses followed the National Center for Health Statistics (NCHS) analytical guidelines to account for the complex survey design [31].

Analyses were conducted using EmpowerStats (version 4.2) and R (version 3.4.3). Continuous data were given as median (Q1-Q3), whereas categorized variables were presented as weighted percentages. To analyze differences in continuous variables among groups, a weighted linear regression model or Kruskal–Wallis nonparametric analysis of variance was applied to the data, while a weighted chi-square test was used for categorical variables. Multiple logistic regression was used to investigate the relationship between hearing threshold or HL and NHHR. Three distinct models were developed: an unadjusted model; a second model adjusted for age, sex, and race; and a third model with further adjustments for PIR, BMI, and diabetes. Smoothed curve fitting and subgroup analyses were also performed.

To control for the potential inflation of type I errors due to multiple comparisons, we applied the Benjamini-Hochberg (BH) correction to the *p*-values generated in the analysis. This correction method was used to adjust for multiple testing in the regression models across different hearing frequencies (low, speech, and high) and HL models, ensuring a controlled false discovery rate while maintaining statistical power.

Results

Characteristics of participation

Table 1 demonstrates how the 4,296 individuals' characteristics were stratified based on NHHR index tertiles. Among the participants, 956 (22.25%) were aged 6–12 years, and 3,340 (77.75%) were aged 13–19 years. This study included 2,252 males (52.42%) and 2,044 females (47.58%). Of the participants, 26 (0.61%) had diabetes, and the median BMI was 22.29 (19.42–26.55) kg/m². The median (Q1-Q3) for low, speech and high-frequency thresholds in no HL group were 5.00 (2.50–8.33) dB, 5.00 (2.50–7.81) dB, and 5.00 (2.50–7.97) dB, respectively. The median (Q1-Q3) for low, speech, and high-frequency thresholds in the HL group were 25.21 (21.25–34.27) dB, 27.97 (23.05–35.16) dB, and 27.08 (21.90-35.35) dB, respectively. In addition, 78 participants (1.81%) had low-frequency HL, 68 (1.58%) had speech-frequency HL, and 70 (1.63%) had high-frequency HL. The detailed characteristics of the participants with HL are presented in Tables 2.

When the NHHR index was divided into tertiles, greater NHHR index values were associated with a greater hearing threshold. In the highest NHHR tertile group, the percentage of participants with HL at all frequencies was significantly higher, with statistically significant differences between groups. This group also had a slightly larger number of men than women and a higher proportion of Mexican Americans and Non-Hispanic White than other races. Additionally, participants in the highest NHHR tertile had higher BMIs and lower PIRs.

Table 1 Participant characteristics according to the tertiles of NHHR index

Characteristics	Overall	Tertiles of NHHR Index			*P*-value
		Tertile 1 (0.406–1.684)	Tertile 2 (1.685–2.364)	Tertile 3 (2.365–8.120)	
Continuous variables, Median (Q1-Q3)	No HL / HL				
Low-frequency PTA (dB)	5.00 (2.50–8.33) / 25.21 (21.25–34.27)	4.58 (2.08–7.92)	5.00 (2.50–7.92)	5.83 (3.33–9.17)	**< 0.001**
Speech-frequency PTA (dB)	5.00 (2.50–7.81) / 27.97 (23.05–35.16)	4.38 (2.19–7.73)	4.69 (2.19–7.81)	5.62 (3.12–8.75)	**< 0.001**
High-frequency PTA (dB)	5.00 (2.50–7.97) / 27.08 (21.90-35.35)	4.64 (2.19–7.76)	4.79 (2.40–7.86)	5.83 (3.07–8.96)	**< 0.001**
PIR	1.65 (0.87–3.25)	1.71 (0.92–3.42)	1.69 (0.88–3.28)	1.55 (0.82–2.99)	**< 0.001**
BMI (kg/m2)	22.29 (19.42–26.55)	20.49 (18.27–23.25)	21.90 (19.38–25.40)	25.78 (21.85–30.78)	**< 0.001**
Categorical variables, %					
Gender N (%)					**< 0.001**
Male	2252 (52.42%)	716 (50.07%)	689 (48.08%)	847 (59.11%)	
Female	2044 (47.58%)	714 (49.93%)	744 (51.92%)	586 (40.89%)	
Age (years) N (%)					**< 0.001**
6–12	956 (22.25%)	365 (25.52%)	324 (22.61%)	267 (18.63%)	
13–19	3340 (77.75%)	1065 (74.48%)	1109 (77.39%)	1166 (81.37%)	
Race N (%)					**< 0.001**
Mexican American	1123 (26.14%)	327 (22.87%)	356 (24.84%)	440 (30.70%)	
Other Hispanic	341 (7.94%)	117 (8.18%)	102 (7.12%)	122 (8.51%)	
Non-Hispanic White	1296 (30.17%)	396 (27.69%)	429 (29.94%)	471 (32.87%)	
Non-Hispanic Black	1129 (26.28%)	442 (30.91%)	400 (27.91%)	287 (20.03%)	
Other Race	407 (9.47%)	148 (10.35%)	146 (10.19%)	113 (7.89%)	
Diabetes N (%)					0.241
Yes	26 (0.61%)	5 (0.35%)	9 (0.63%)	12 (0.84%)	
No	4270 (99.39%)	1425 (99.65%)	1424 (99.37%)	1421 (99.16%)	
Low-frequency HL N (%)					**0.001**
No	4218 (98.18%)	1411 (98.67%)	1415 (98.74%)	1392 (97.14%)	
Yes	78 (1.81%)	19 (1.33%)	18 (1.26%)	41 (2.86%)	
Speech-frequency HL N (%)					**0.011**
No	4228 (98.42%)	1411 (98.67%)	1418 (98.95%)	1399 (97.63%)	
Yes	68 (1.58%)	19 (1.33%)	15 (1.05%)	34 (2.37%)	
High-frequency HL N (%)					**0.002**
No	4226 (98.37%)	1413 (98.81%)	1417 (98.88%)	1396 (97.42%)	
Yes	70 (1.63%)	17 (1.19%)	16 (1.12%)	37 (2.58%)	

For categorical variables: survey-weighted percentage (95% CI), *P*-value was by survey-weighted Chi-square test

Footnote:

Low-frequency: averaged of 0.5, 1, 2 kHz

Speech-frequency: averaged of 0.5, 1, 2, 4 kHz

High-frequency: averaged of 4, 6, 8 kHz

BMI: Body Mass Index; PIR: Income-Poverty Ratio; PTA: Pure-Tone Audiometry

Associations between the NHHR index and auditory threshold

The findings demonstrated a relationship between the NHHR and variations in hearing thresholds across all frequencies (Table 3). In the unadjusted models, each unit increase in the NHHR index has a regression coefficient of 0.65 for hearing thresholds, indicating a significant positive correlation between NHHR and hearing thresholds. After controlling for sex, age, and race, Model II revealed a positive correlation between the NHHR and hearing threshold changes at all frequencies. To further reduce the impact of additional confounding variables, the covariates from Model II were retained, and adjustments for PIR, BMI, and diabetes were incorporated in Model III. The NHHR index showed a positive connection with hearing threshold alterations, including low-frequency (β:0.37; 95% CI: 0.16–0.58), speech-frequency (β:0.32; 95% CI: 0.12–0.5), and high-frequency (β:0.35; 95% CI: 0.14–0.55).

Table 2 Participant characteristics according to hearing loss (HL)

Characteristics	Low-frequency HL			Speech-frequency HL			High-frequency HL		
	No	Yes	*P*-value	No	Yes	*P*-value	No	Yes	*P*-value
N	4218	78		4228	68		4226	70	
Median (Q1-Q3)	5.00 (2.50–8.33)	25.21 (21.25–34.27)		5.00 (2.50–7.81)	27.97 (23.05–35.16)		5.00 (2.50–7.97)	27.08 (21.90-35.35)	
***Continuous variables*, Median (Q1-Q3)**									
BMI (kg/m^2)	22.25 (19.41–26.50)	24.01 (20.14–30.12)	0.017	22.26 (19.42–26.50)	23.22 (19.99–29.05)	0.107	22.26 (19.42–26.50)	23.66 (19.76–29.90)	0.077
PIR	1.65 (0.87–3.25)	1.50 (0.88–2.88)	0.629	1.65 (0.87–3.25)	1.58 (0.93–2.91)	0.800	1.65 (0.88–3.25)	1.58 (0.86–3.04)	0.657
NHHR	1.98 (1.53–2.60)	2.49 (1.71–3.38)	< 0.001	1.98 (1.53–2.60)	2.34 (1.63–3.24)	0.003	1.98 (1.53–2.60)	2.48 (1.73–3.33)	< 0.001
***Categorical variables*, N (%)**									
Gender			0.104			0.287			0.200
Male	2204 (52.25%)	48 (61.54%)		2212 (52.32%)	40 (58.82%)		2210 (52.30%)	42 (60.00%)	
Female	2014 (47.75%)	30 (38.46%)		2016 (47.68%)	28 (41.18%)		2016 (47.70%)	28 (40.00%)	
Age (years)			0.709			0.969			0.903
6–12	940 (22.3%)	16 (20.5%)		941 (22.3%)	15 (22.1%)		940 (22.2%)	16 (22.9%)	
13–19	3278 (77.7%)	62 (79.5%)		3287 (77.7%)	53 (77.9%)		3286 (77.8%)	54 (77.1%)	
Race			0.078			0.476			0.214
Mexican American	1110 (26.32%)	13 (16.67%)		1111 (26.28%)	12 (17.65%)		1112 (26.31%)	11 (15.71%)	
Other Hispanic	330 (7.82%)	11 (14.10%)		335 (7.92%)	6 (8.82%)		334 (7.90%)	7 (10.00%)	
Non-Hispanic White	1274 (30.20%)	22 (28.21%)		1275 (30.16%)	21 (30.88%)		1275 (30.17%)	21 (30.00%)	
Non-Hispanic Black	1103 (26.15%)	26 (33.33%)		1106 (26.16%)	23 (33.82%)		1104 (26.12%)	25 (35.71%)	
Other Race	401 (9.51%)	6 (7.69%)		401 (9.48%)	6 (8.82%)		401 (9.49%)	6 (8.57%)	
Diabetes			0.487			0.517			0.510
Yes	26 (0.62%)	0 (0.00%)		26 (0.61%)	0 (0.00%)		26 (0.62%)	0 (0.00%)	
No	4192 (99.38%)	78 (100.00%)		4202 (99.39%)	68 (100.00%)		4200 (99.38%)	70 (100.00%)	

Footnote:

Low-frequency: averaged of 0.5, 1, 2 kHz

Speech-frequency: averaged of 0.5, 1, 2, 4 kHz

High-frequency: averaged of 4, 6, 8 kHz

BMI: Body Mass Index; PIR: Income-Poverty Ratio; PTA: Pure-Tone Audiometry

To improve the reliability of the outcomes, a sensitivity analysis was performed by dividing the NHHR scores into tertiles. Results were statistically significant. Notably, in the low-frequency, speech-frequency, and high-frequency hearing thresholds, the β values were higher for individuals in the highest NHHR index tertile compared to those in the lowest tertile, with a *P* for trend less than 0.05. (Table 3).

To further eliminate the influence of diabetes and BMI on the correlation between NHHR and hearing, a correlation analysis was conducted excluding individuals with diabetes. The results are shown in Supplementary Materials Table 3-1 and Table 3-2. Additionally, another analysis was performed excluding both individuals with diabetes and those with a BMI greater than 30. The results are shown in Supplementary Materials Table 4-1 and Table 4-2. This re-evaluation confirms that the association between NHHR and both hearing threshold levels and HL remains statistically significant, although the strength of the association slightly decreases after

Table 3 Logistic regression analysis between NHHR index with hearing-frequency prevalence

Characteristics	β (95% CI) *P* value of PTA levels, dB		
	Model 1	Model 2	Model 3
Low-frequency PTA			
NHHR Index	0.65 (0.46, 0.84) < 0.0002	0.56 (0.36, 0.75) < 0.0002	0.37 (0.16, 0.58) 0.0013
NHHR Tertile			
Low (0.406–1.684)	Reference	Reference	Reference
Middle (1.685–2.364)	0.64 (0.22, 1.07) 0.0041	0.65 (0.22, 1.07) 0.0041	0.53 (0.10, 0.96) 0.0157
High (2.365–8.120)	1.32 (0.89, 1.75) < 0.0002	1.13 (0.70, 1.57) < 0.0002	0.71 (0.25, 1.17) 0.0041
P for trend	< 0.0002	< 0.0002	0.0041
Speech-frequency PTA			
NHHR Index	0.66 (0.47, 0.85) < 0.0002	0.55 (0.36, 0.74) < 0.0002	0.32 (0.12, 0.53) 0.0090
NHHR Tertile			
Low (0.406–1.684)	Reference	Reference	Reference
Middle (1.685–2.364)	0.63 (0.21, 1.05) 0.0041	0.63 (0.21, 1.05) 0.0041	0.50 (0.08, 0.91) 0.0201
High (2.365–8.120)	1.32 (0.90, 1.74) < 0.0002	1.10 (0.68, 1.53) < 0.0002	0.61 (0.16, 1.06) 0.0130
P for trend	< 0.0002	< 0.0002	0.0041
High-frequency PTA			
NHHR Index	0.66 (0.47, 0.84) < 0.0002	0.55 (0.36, 0.74) < 0.0002	0.35 (0.14, 0.55) 0.00198
NHHR Tertile			
Low (0.406–1.684)	Reference	Reference	Reference
Middle (1.685–2.364)	0.64 (0.22, 1.06) 0.0041	0.64 (0.22, 1.06) 0.0041	0.51 (0.09, 0.93) 0.0168
High (2.365–8.120)	1.32 (0.90, 1.74) < 0.0002	1.12 (0.69, 1.54) < 0.0002	0.66 (0.21, 1.11) 0.0052
P for trend	< 0.0002	< 0.0002	0.0075

Model 1: No adjustment for co-variables; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, BMI, PIR, diabetes

Table 4 Logistic regression analysis between NHHR index with HL

NHHR Index	OR (95% CI) *P* value of HL		
	Model 1	Model 2	Model 3
Low-frequency HL	1.47 (1.21, 1.77) < 0.0003	1.49 (1.22, 1.80) < 0.0003	1.35 (1.08, 1.69) 0.0102
Speech-frequency HL	1.43 (1.16, 1.75) 0.0011	1.46 (1.18, 1.80) 0.0009	1.36 (1.07, 1.73) 0.0130
High-frequency HL	1.47 (1.20, 1.79) 0.00045	1.50 (1.23, 1.84) < 0.0003	1.39 (1.10, 1.76) 0.0071

Model 1: No adjustment for co-variables, Model 2: Adjusted for age, gender, race, Model 3: Adjusted for age, gender, race, BMI, PIR, diabetes

excluding the diabetic and obese populations. These findings suggest that while diabetes and BMI may influence the relationship, NHHR still independently contributes to HL risk.

Moreover, to account for the potential influence of noise exposure on the NHHR-hearing correlation, a re-analysis was conducted with noise exposure included as a covariate. The results are provided in Supplementary Materials Table 5-1 and Table 5-2. This additional analysis similarly confirms that the association between NHHR and both hearing threshold levels and HL remains statistically significant, although the strength of the association decreases slightly when noise exposure is considered. Overall, these findings suggest that NHHR independently contributes to HL risk, even when controlling for diabetes, BMI, and noise exposure.

Associations between NHHR index and HL

Weighted logistic regression was used to investigate the possible connections between HL status and the NHHR index. In the analysis with HL as the outcome, NHHR is positively correlated with HL across all frequencies, low-frequency (OR:1.35, 95% CI: 1.08, 1.69;); Speech-frequency (OR:1.36, 95% CI: 1.07, 1.73); High-frequency (OR:1.39, 95% CI: 1.10, 1.76). (Table 4). To control for the potential inflation of type I errors due to multiple comparisons, the BH correction was applied to the *p*-values. The corrected *p*-values are provided in the supplementary materials.

Relationship between NHHR index and hearing threshold visualization

A smoothed curve fit was used to illustrate the association between the NHHR and hearing threshold at three frequencies, with the necessary variables controlled for. (Fig. 2). ln-transformation of NHHR helped to smooth the curve and stabilize the fitting, particularly in the higher NHHR values (Supplementary Materials Figs. 2-1). The analysis revealed a general dose-response relationship between the NHHR and the average hearing thresholds at low, speech, and high frequencies.

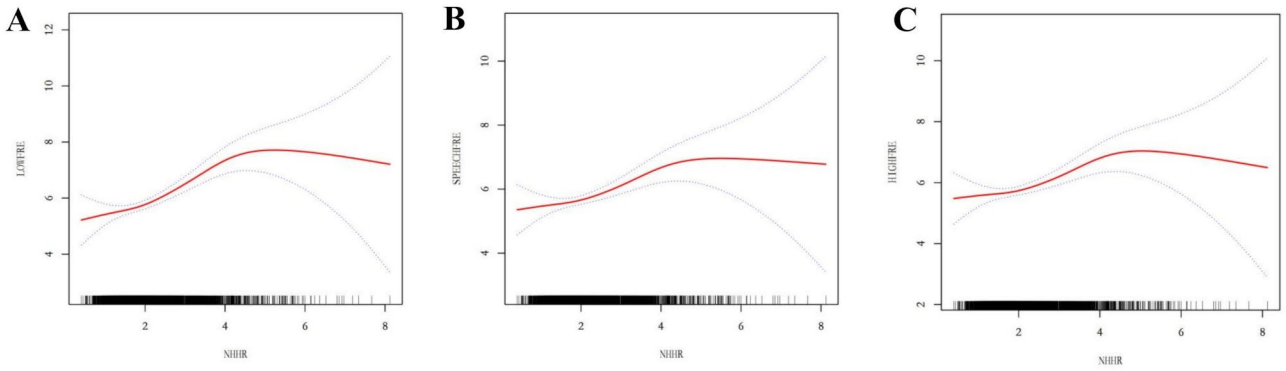

Fig. 2 Relationship between NHHR and hearing threshold shifts. Panel **A**: Low-frequency Pure Tone Audiometry (PTA). Panel **B**: Speech-frequency PTA. Panel **C**: High-frequency PTA. Each panel displays a smoothed red line representing the median hearing threshold shift, accompanied by dotted grey lines depicting the 95% confidence intervals. The x-axis represents the NHHR values, while the y-axis shows hearing threshold levels measured in decibels (dB). Below each graph, histograms illustrate the distribution of NHHR values among the study population. This analysis emphasizes how various NHHR levels correlate with hearing sensitivity across different frequency ranges

Subgroup analyses

Figure 3 presents an examination of the NHHR for speech-frequency PTA according to sex, age, race, PIR, BMI, and diabetes. Interaction tests revealed no significant differences in the relationship between the NHHR and speech frequency among the subgroups. The covariates included in the adjustments did not have a significant effect on favorable associations. ($P>0.05$) for all interactions.

Discussion

The NHHR was selected as the primary indicator. NHHR is a recently discovered composite biomarker of atherogenic lipids [32]. The NHHR measures harmful (LDL-C and VLDL-C) and beneficial (HDL-C) lipoproteins and offers a comprehensive view of lipid abnormalities suitable for large-scale screening. Compared to standard lipid parameters, the NHHR offers an improved assessment of cardiovascular and cerebrovascular disease risk [18]. Unlike TyG, which focuses on insulin resistance, and AIP, which targets lipid imbalance, the NHHR provides a broader assessment of cardiovascular health. This makes the NHHR useful for exploring its correlation with adolescent hearing health and identifying early risk factors.

This study assessed the association between NHHR and hearing in American adolescents. After controlling for variables, NHHR was associated with a higher prevalence of HL across all frequency categories. Furthermore, a linear dose-dependent association was found between NHHR and hearing thresholds at all frequencies. Subgroup analysis indicated that factors such as sex, age, race, PIR, BMI, and diabetes did not appear to have a substantial impact on favorable connections.

NHHR is a unique lipid ratio that can be used to assess atherogenic lipid levels. While no prior studies have specifically examined NHHR's role in HL, a broader association between lipids and hearing function is well documented. A retrospective study indicated a positive correlation between fasting plasma cholesterol levels and elevated hearing thresholds [33]. Early studies found that the triglyceride–glucose (TyG) index and atherogenic index of plasma (AIP) positively correlate with HL, particularly at high frequencies [34–36]. This may be related to differences in lipid metabolism and oxidative energy supply between Hensen's cells of the cochlear apex and the basal turn [37]. The TyG showed a nonlinear relationship with speech and high-frequency thresholds [15]. These findings suggest that abnormalities in lipid metabolism affect hearing. However, these studies have focused on adults, and similar research on adolescents is lacking. Mixed outcomes in teenagers may be attributed to individual differences, ethnic diversity, and variations in the timing and methodology of lipid and hearing assessments [38]. Some studies have suggested that blood lipid levels do not effectively predict hearing threshold levels [38, 39]. Evidence that hyperlipidemia causes hearing problems is contradictory [40]. However, the inconsistency in sample sizes, population heterogeneity, and differing focus on metrics may have influenced the results. Nonetheless, given the importance of lipid metabolism in the normal function of the inner ear, further research and exploration of its impact on inner ear function are critical.

The continuous and categorical models showed a positive association, however, these results should be interpreted with caution. HL can be influenced by multiple factors, including genetics, environment, and medication. While there is a positive association between NHHR and hearing thresholds and HL, it is important not to overemphasize the direct effect of NHHR on HL in clinical decision-making. NHHR is just one aspect influencing

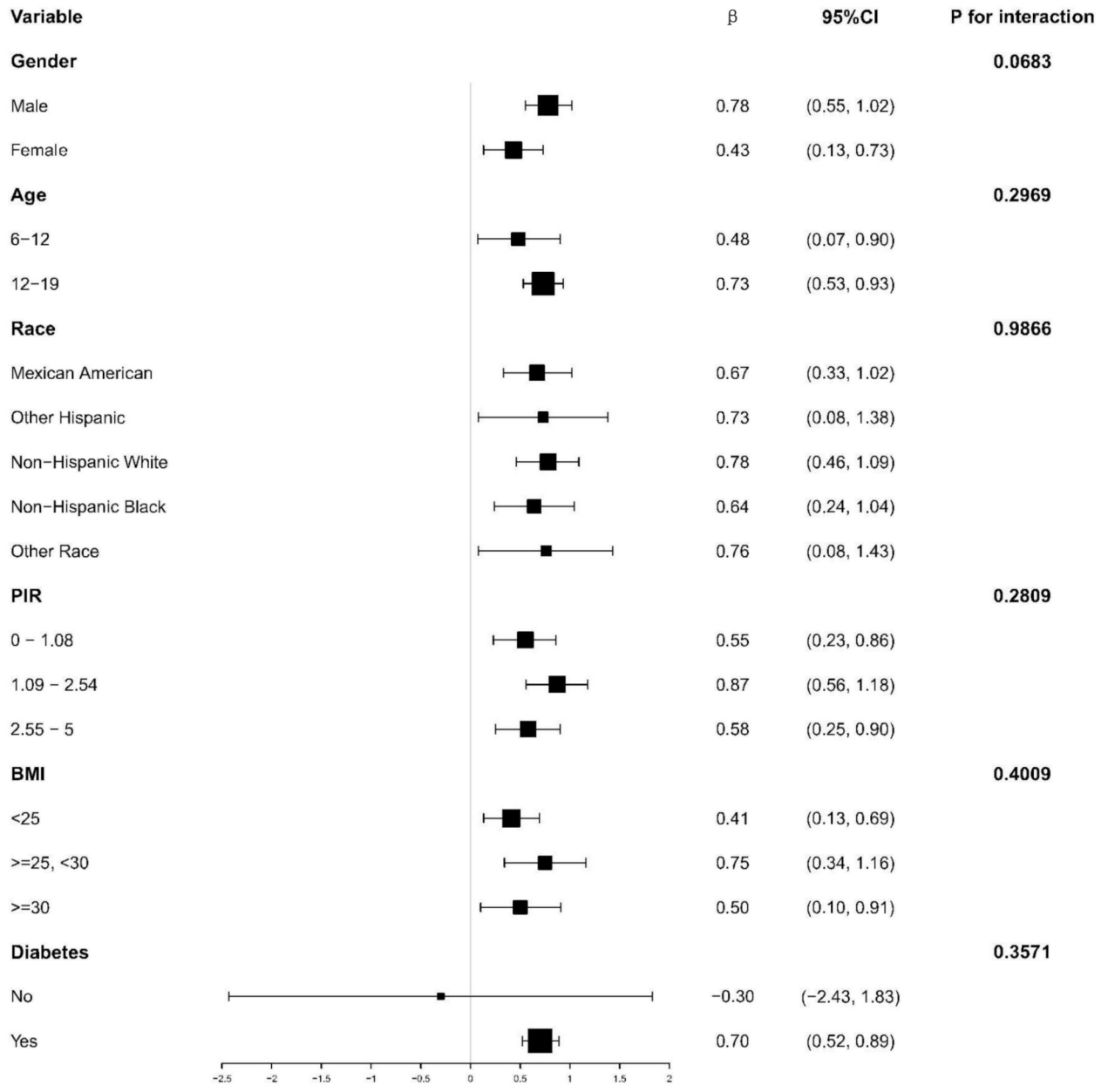

Fig. 3 Impact of NHHR on speech-frequency PTA by subgroups. This forest plot illustrates the association between the NHHR and speech-frequency PTA across various factors, including gender, age, race, PIR, BMI, and diabetes. Each point represents the regression coefficient (β), with bars indicating 95% confidence intervals. The *P*-values for interaction are also provided to assess the statistical significance of differences between groups. The inclusion of covariates in the adjustments did not significantly alter the positive association observed (all interaction *p*-values > 0.05)

hearing. However, it does highlight the significance of maintaining lipid homeostasis for hearing health.

Few studies have investigated the mechanisms that link lipid profiles to hearing. Dyslipidemia can cause microcirculatory disturbances in the cochlea [19, 20]. Stenosis of the spiral modiolar artery (SMA) can cause ear ischemia, low oxygen levels, impaired endothelial function, and reduced eNOS activity, potentially leading to hearing damage [41]. Dyslipidemia may also alter cellular lipid components and increase reactive oxygen species (ROS) production [42, 43]. Accumulated oxidative damage in mitochondria due to ROS can cause mitochondrial dysfunction and apoptosis [44, 45]. Researchers used an apolipoprotein E-knockout (ApoE-KO) mouse model fed a high-cholesterol diet to study this mechanism. Compared with wild-type mice, ApoE-KO mice

exhibit significant hyperlipidemia, atherosclerosis, endothelial dysfunction, and hearing impairment, indicating that hyperlipidemia can alter cochlear morphology and function [41]. It has been suggested that cholesterol is crucial for inner ear function, and both excessive and insufficient levels are harmful [46]. Hypercholesterolemia-related hearing impairment may lead to DPOAE abnormalities before hearing threshold changes [47]. The outer hair cells (OHC), which are most sensitive to injury, are also affected by lipid disorders. The properties of the OHC plasma membrane, including its lipid makeup, fluidity, and stiffness, are essential for maintaining the normal electromotive function and operation of the cochlear amplifier [48]. The lipid component of the OHC lateral wall plasma membrane plays a crucial role in generating electromotility [49]. Therefore, it is hypothesized that outer hair cells may be especially vulnerable to dyslipidemia.

This study identifies NHHR as a potential biomarker for the early detection of adolescents at risk for HL, providing a reference value for integrating lipid management into routine health assessments for preventive care. By recognizing the link between dyslipidemia and HL, it offers early detection assessments and explores the possibility of promoting cardiovascular health to potentially reduce the risk of hearing damage. The study emphasizes the importance of educating patients, families, and healthcare professionals about the interaction between lipid profiles and hearing health to encourage healthier lifestyle choices.

Strengths and limitations

The primary advantage of our study is the use of a large, nationally representative group of US adolescents. To guarantee reliable results, several variables were evaluated and confounding variables were controlled for. However, this study has several limitations. First, the cross-sectional design prevented us from determining the causal relationship between NHHR and HL. Second, the observed association between NHHR and HL raises concerns about the direction of causality. Third, only fasting cholesterol data were used, which may introduce bias compared with non-fasting data. Fourth, although noise exposure was included as a covariate, the significant amount of missing data warrants cautious interpretation of the results. Noise is a known factor in hearing loss and may interact with metabolic health. Further research is needed to explore their combined effects on hearing.

These limitations suggest that although the findings are insightful, the current results need to be interpreted cautiously. Further validation through prospective studies and randomized controlled trials is required to confirm these observations and explore the underlying mechanisms linking the NHHR to auditory health.

Conclusions

The study confirmed that the NHHR is associated with a higher risk of increased hearing thresholds among adolescents in the USA. Given the increasing prevalence of dyslipidemia among young people, the study highlights the importance of early lipid monitoring and management as strategies to prevent or reduce hearing impairment. Additional prospective studies and randomized controlled trials are required to confirm these findings. Further research is needed to better understand the underlying processes and investigate potential treatment strategies.

Abbreviations

AIP	Atherogenic Index of Plasma
ApoE-KO	Apolipoprotein E Knockout
BH	Benjamini-Hochberg
BMI	Body Mass Index
DPOAE	Distortion Product Otoacoustic Emissions
HDL-C	High-Density Lipoprotein Cholesterol
HL	Hearing Loss
IDL	Intermediate-Density Lipoprotein
LDL-C	Low-Density Lipoprotein Cholesterol
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NHHR	Non-High-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol Ratio
OHC	Outer Hair Cells
OR	Odds Ratio
PIR	Poverty Income Ratio
PTA	Pure-Tone Audiometry
ROS	Reactive Oxygen Species
SMA	Spiral Modiolar Artery
SNHL	Sensorineural Hearing Loss
SSNHL	Sudden Sensorineural Hearing Loss
TyG	Triglyceride-Glucose Index
VLDL	Very Low-Density Lipoprotein
WTMEC2YR	Weighting Variable for the 2-year MEC Exam Weight

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02331-6.

Supplementary Material 1: Table 3-1

Supplementary Material 2: Table 3-2

Supplementary Material 3: Table 4-1

Supplementary Material 4: Table 4-2

Supplementary Material 5: Table 5-1

Supplementary Material 6: Table 5-2

Supplementary Material 7: Figure 2-1

Acknowledgements

We extend our gratitude to all NHANES participants.

Author contributions

Conception: Zhe Peng and Shusheng Gong. Methodology: Zhe Peng and Qian Wu. Data curation by Zhe Peng, Chunli Zhao, and Qian Wu. The formal analysis includes Zhe Peng, Qian Wu, Chunli Zhao, and Shusheng Gong. Zhe Peng and Shusheng Gong are responsible for the first drafting. Zhe Peng and Shusheng Gong handled the revision and editing. Funding acquisition:

Zhe Peng and Shusheng Gong. All authors evaluated and approved the final version of the text.

Funding
The work was sponsored by the Natural Science Foundation of Capital Medical University (grant number PYZ23078) and the National Natural Science Foundation of China (grant number 82171131).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by NCHS Research Ethics Review Board (ERB). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Consent for publication
Relevant data from participants were collected from the publicly accessible NHANES database, eliminating the need for obtaining additional consent.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Otolaryngology-Head and Neck Surgery, Beijing Friendship Hospital, Capital Medical University, No.95, Yong'an Road, Xicheng District, Beijing 100050, China
[2]Clinical Center for Hearing Loss, Capital Medical University, Beijing 100050, China

Received: 19 June 2024 / Accepted: 14 October 2024
Published online: 19 October 2024

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