Higher serum magnesium concentration is associated with lower hearing thresholds and risk of hearing loss among a Chinese population

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ABSTRACT

Background and Objectives: Hearing loss is a sensory impairment caused by genetic and environmental factors. Previous epidemiological studies of magnesium intake and hearing loss have been conflicting. **Methods and Study Design:** We investigated the association between serum magnesium concentrations and hearing loss in a population in Zhejiang region in China. A cross-sectional study of 3,267 participants aged 18 years and above from five hospitals was conducted from October 2016 to May 2018. Audiometric examination was conducted, and hearing thresholds as pure-tone averages (PTAs) at speech (0.5, 1, 2, and 4 kHz) and at high frequencies (3, 4, and 6 kHz) were computed. Magnesium concentrations were measured using an inductively coupled plasma mass spectrometer. **Results:** We found a negative association between magnesium levels and hearing loss from lower PTA to high PTA by linear regression analysis. After adjustment of potential confounders, participants in the highest quartile of magnesium had lower PTA (quartile 4: −1.89%; 95% confidence interval (CI: −3.07 to −0.701; p=0.022) and high PTA (quartile 4: −3.05%; 95% CI: −4.64 to −1.46; p=0.005) than those in the lowest quartile. Logistic regression analysis showed a dose-dependent reduction in the odds of high frequency hearing loss across quartiles of magnesium. In model 3, after adjusting for all potential confounders, participants with the highest quartiles of magnesium had a 54.0% (OR: 0.460; 95% CI: 0.339–0.587) reduction in the odds of high frequency hearing loss. **Conclusions:** Higher levels of whole blood magnesium in this population were associated with lower hearing thresholds and risk of hearing loss.

Key Words: magnesium, hearing loss, population, cross-sectional study, linear regression analysis

INTRODUCTION

Hearing loss is a major public health problem and is the fifth leading cause of living with disability, ahead of many other chronic diseases, such as diabetes, dementia, and chronic obstructive pulmonary disease.[1,2] According to the World Health Organization, 3.6 million patients worldwide have hearing loss.[3] The Global Burden of Disease study estimated that adult-onset hearing loss was the third leading cause of disability.[4] Hearing loss is regarded as not only a communication disability, but also a major disease that severely impairs patient's quality of life, due to social withdrawal, psychological alienation, loss of confidence increased depression, and anxiety.[5] Therefore, it is important to identify protective factors and avoid risk factors to prevent these negative effects.

Hearing loss is caused by genetic and environmental factors.[6,7] However, only a few studies have evaluated patients with hearing loss, and there is limited public awareness on the causes and effects of hearing loss. Recent epidemiological studies showed that nutritional status was associated with hearing loss.[8] It was also reported that higher intake of antioxidant vitamins (β-carotene, vitamins C, and vitamin E) and magnesium are associated with lower risks of hearing loss in the US general population.[9] Attias J et al provided evidence that magnesium intake was associated with lower temporary threshold shift in humans.[10] Indeed, many animal experiments revealed that magnesium supplementation could reduce or slow down noise-induced hearing loss (NHL).[10-12] Reports showed that free radical formation in the inner ear causes cell death and vasoconstriction and a rebound in cochlear blood flow, which was associated with hearing loss, suggested that antioxidants may play a preventive role in hearing loss.[13,14] However, some epidemiological studies that evaluated the relationship between magnesium and hearing loss revealed inconsistent results. A previous study showed that serum magnesium ion level may not be associated with NHL.[15] In this study, we aimed to evaluate the association between magnesium concentration in whole blood and hearing loss based on a cross-sectional study in a population of Zhejiang region in China. Through this research, we can provide nutrition-related health education to prevent hearing loss in the healthy population.

MATERIALS AND METHODS

Participants

Between October 2016 and May 2018, 3,500 adults aged 18 years and older who attended a medical examination in five different hospitals (Jianshan People's Hospital, Anji People's Hospital, Jinyun People's Hospital, Jiaxin Armed police hospital, and Tonglu People's Hospital) in Zhejiang Province, China, were recruited in this study. All participants were informed about the study and signed an informed consent form for the hearing survey. The study was approved by the ethics committee of Hangzhou Normal University (2017LL107) and all procedures were performed in accordance with the Declaration of Helsinki. Participants (1) who currently have or had a history of otitis media; (2) with hereditary hearing loss; (3) with history of occupational noise exposure; (4) with missing data on age, gender, family history of hearing loss, or other key variables; and (5) who were unresponsive or exhibited unreliable response during audiometric examinations were excluded. Additionally, 204 adults and 29 participants who refused to provide blood samples were also excluded from the analysis. Finally, 3,267 participants were enrolled in our study.

Sample collection

The blood samples were collected in ethylenediaminetetraacetic acid tubes from all participants. Specimens collected were coded by a unique identification number. All specimens were stored at -70°C until testing.

Questionnaires

Participants' data on age, gender, marriage (single, married, divorced, and widowed), education (elementary school, middle school, high school, college, and postgraduate), and personal monthly income (≤2,000 yuan, 2001-4000 yuan, 4000-6000 yuan, 6001-8000 yuan, and ≥8000 yuan) were obtained based on the standard format. Self-reported family history of hearing loss, hypertension, cigarette smoking, alcohol drinking, sleeping time, and noise exposure were also collected in the same format. Hypertension was defined as a self-reported physician diagnosis, current use of antihypertensive medication, systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg at the time of examination. A participant was categorized as a current smoker if he smoked at least one cigarette per week or alcohol drinker if he drank at least once per week. Sleeping time (<4 hours, 4-6 hours, 6-8 hours, and ≥8 hours) was also included in the questionnaire. Occupational noise exposure was defined as exposure to loud noise in the workplace at least once a week, while living noise exposure was defined as exposure to loud noise outside of workplace at least once a week.

Audiometric examination

A Madsen Itera clinical diagnostic audiometer and TDH39 headphones (GN Otometrics, Denmark) were used in audiometric examination by trained technicians in a sound-proof chamber with noise levels below 30 dB.16 Pure-tone air conduction thresholds were determined for each ear from 0.5 to 8 kHz across an intensity range of −10 to 120 dB. Hearing loss at the low frequencies was defined as a pure-tone average (PTA) of more than 25 dB at 0.125 and 0.25 kHz (low PTA) in the worse ear. Speech frequency hearing loss was defined as a pure-tone average of more than 25 dB at 0.5, 1, and 2 kHz (speech PTA) in the worse ear. A PTA of more than 25 dB at 3, 4, 6, and 8 kHz (high PTA) in the worse ear indicates high-frequency hearing loss.[17] In the audiometric examination, participants who did not respond at least once were considered as nonresponsive. In order to measure the reliability of the participants' response, the 1-kHz frequency was tested twice in each ear. If the results were more than 10 dB, it was considered to be an unreliable response.[18]

Measurement of magnesium concentration in whole blood

Magnesium concentrations in venous whole blood were measured by a standard seven-trace elements test kit (Bohui Innovation Photoelectric Technology Co., Ltd, Beijing) using an inductively coupled plasma mass spectrometer (ICP-MS, Thermo Electron Corporation, USA). Quality control was performed using samples prepared in the laboratory and standard materials (Norwegian Semnorm Company) in the detection process (CV <6.67%).

Statistical analysis

Data analysis was performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive analyses and distribution of all key variables were conducted. Survey t-test and analysis of variance tests were used to analyze continuous variables. The Chi-square test and the Kruskal-Wallis test were used for categorical groups. Linear regression and logistic regression were tests used to evaluate the association between magnesium in quartile with hearing thresholds in PTA and hearing loss. All regression models were constructed based on the magnesium concentration to observe the effects of blood magnesium by adjusting different covariates in the models. In model 1, we adjusted age, gender, marriage, educational, personal income, hearing loss family history, and hypertension. In model 2, we included smoking, drinking, and sleeping time as additions to model 1 to determine the influence on the association between blood magnesium and hearing loss. In model 3, occupational noise exposure and living noise exposure were included as additions to model 2. Odds ratios (ORs) and 95% confidence intervals (CIs) for hearing loss were calculated for each of the upper three quartiles of magnesium levels relative to the lowest quartile using logistic regression. Statistical significance was defined as $p<0.05$.

RESULTS

Study participants

A total of 3,267 adults participated in the study. Table 1 summarizes the characteristics of the study cohort. The mean (±SEM) age of the participants was 50.0±15.8 years, average whole blood magnesium concentration was 1.46±0.14 mmol/L, and means of low PTA, speech PTA, and high PTA were 27.0±13.1, 25.6±13.7, and 33.1±19.3 dB, respectively. Approximately 40.4%, 36.1%, and 53.8% of participants had low-frequency, speech-frequency, and high-frequency hearing loss, respectively.

The distribution of magnesium levels in the cohort is presented in Table 2. There was a significant difference in blood concentration of magnesium among groups based on age, gender, education levels, and income levels ($p<0.001$). The levels of magnesium were affected by smoking and drinking ($p<0.001$). There was no difference in PTA among different age and noise exposure groups.

Relationship between magnesium level and hearing threshold

Linear regression analysis showed that the serum magnesium concentrations in quartiles were negatively associated with lower-PTA to high-PTA (Table 3). Compared with participants with the lowest quartile, those with the highest quartile of magnesium had a significant reduction in PTA after adjustment of confounders, such as age, gender, marriage, education, income, and hypertension (model 1). The reduction in speech PTA and high PTA remained significant after further adjustment in model 2 (additional adjustment for smoking, drinking, and sleeping time) and model 3 (additional adjustment for life noise and occupational noise exposure). In patients with low PTA, a significant reduction was only observed in model 3 but not in model 2.

Relationship between magnesium level and risk of hearing loss

Logistic regression showed that higher concentrations of magnesium were associated with lower risk of high-frequency hearing loss (Table 4). After adjustment of age, gender, marriage, education, income, and hypertension (model 1), those with the fourth quartile levels of serum magnesium had 55.0% (OR: 0.450, 95% CI: 0.344–0.590) lower risk of high frequency hearing loss (model 1) than those with the lowest quartile level of blood magnesium, which remained significant after further adjustment of other covariances (models 2 and 3). No significant association was found between speech and low-frequency hearing loss.

DISCUSSION

In this study, we found that more than half of the participants had high-frequency hearing loss and more than a third of participants had speech-frequency hearing loss, which is often ignored because most of the hearing loss does not affect daily communication. Moreover, high-frequency hearing loss frequently occurs in most patients with hearing problems, which should be paid more attention.[19]

Only a few epidemiologic studies reported the protective association between blood magnesium and hearing loss. A previous study of 7,445 workers reported that serum magnesium ion level may not be associated with NHL.[15] Our results found the apparent protective dose-response relations between whole blood magnesium and speech-frequency and high-frequency hearing thresholds by linear regression and ORs of high-frequency hearing loss after adjusting for demographic factors, noise exposures, and other potential risk factors by logistic regression. Several animal studies have also shown that magnesium has a protective effect on hearing loss.[20] Prell et al found that dietary supplements containing magnesium protected the function and morphology of hair cells in the inner ear of mice exposed to noise.[21,22] Another previous study found that hearing loss in guinea pigs was reduced after receiving dietary antioxidants delivered in combination with magnesium, suggesting that magnesium and other antioxidants protected hearing by inhibiting free radicals.[23,24]

Free radicals, which can be induced by noise exposure and cause cell injury and cell death in the inner ear, may play a critical role in the negative association between blood magnesium and risk of hearing loss.[20] Despite extensive basic research evidence and results from animal studies, it is extremely important to carefully examine the prophylactic effects of magnesium on human participants before preventing or implementing the use of this supplement, given the differences in human and animals. In a controlled clinical trial conducted by David et al, magnesium can also influence hearing directly, by increasing blood viscosity and blood flow, or indirectly, via its effects on the cell energy cycle. Magnesium treatment improved the hearing of patients with sudden sensorineural hearing loss.[25] Choi et al suggested that magnesium intake along with antioxidants was associated with lower risks of hearing loss in humans.[9] Moreover, oral magnesium intake may reduce NHL.[26] These studies provide the scientific rationale to support our findings.

To our knowledge, this is the first population-based epidemiological study to report the association between magnesium and hearing loss. However, the study also has several potential limitations. First, many influential factors were obtained through self-reporting, e.g., hypertension, socioeconomic data, and occupational noise exposure, which could potentially contain measurement errors. Second, the hearing threshold was determined using the ear that performed worse, which led to the increase in the prevalence of hearing loss. Third, the study only included those in the Chinese Han population. Thus, it is not certain whether the study will yield the same results in other ethnic groups. Lastly, because this is a cross-sectional study, the cause-and-effect relationship cannot be inferred nor can reverse causation and other mechanisms be ruled out.

We found that higher levels of whole blood magnesium were associated with lower hearing thresholds and risk of hearing loss, even after adjusting for confounding factors. Therefore, we believe that dietary or nutritional supplements rich in magnesium may be effective in preventing hearing loss. In addition, this study provides an epidemiological basis for the clinical application of magnesium therapy for hearing loss. In further research, we will examine the continuous magnesium concentration in the blood of this population to affirm the association with hearing loss. Then, we will provide nutrition-related health education for the prevention of hearing loss in the normal population.

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AUTHOR DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Characteristics of the study population (n=3267)[†]

Characteristic	Distribution
Age	50.0±15.8
Gender	
Male	47.00%
Female	53.00%
Marriage status	
Single	7.50%
Married	89.10%
Divorce	1.90%
Bereft of one's spouse	1.50%
Education level	
≤Elementary school	14.90%
Middle school	22.80%
High school	25.30%
College	36.00%
Postgraduate	1.00%
Income (yuan)	
≤2000	14.00%
2001-4000	23.60%
4001-6000	36.90%
6001-8000	14.00%
≥8001	4.40%
Hearing loss family history	
No	87.00%
Yes	13.00%
Hypertension	
No	77.80%
Yes	20.10%
Smoking	
Never	77.20%
Former	5.90%
Current	16.90%
Alcohol drinking	
Never	84.30%
Former	2.10%
Current	13.60%
Sleeping time	
＜4 hours	1.00%
4-6 hours	4.70%
6-8 hours	65.10%
≥8 hours	29.20%
Living noise exposure	
Never	76.30%
At least once a week	15.30%
At least once a day	8.40%
Occupational noise exposure	
Never	62.50%
At least once a week	26.80%
At least once a day	10.70%
Mg(umol/L)	1.46±0.14
Low frequency PTA[‡] (dB)[§]	27.04±13.08
Any low-frequency hearing loss[§]	40.4%
Speech frequency PTA (dB)[¶]	25.65±13.74
Any Speech-frequency hearing loss[¶]	36.10%
High-frequency PTA (dB)[††]	33.12±19.34
Any high-frequency hearing loss[††]	53.80%

[†]Participants included individuals with all variables of interest: age, gender, marriage status, education level, income, hearing loss family history, hypertension, smoking, Alcohol drinking, sleeping time, living noise exposure, occupational noise exposure and magnesium concentration at different frequency PTA.[‡] PTA: pure-tone average. [§]At 0.125, 0.25 kHz. [¶]At 0.5, 1, 2 kHz. [††]At 3, 4, 6, 8 kHz.

Table 2. Blood magnesium concentrations stratified by different groups (n=3267) †

Characteristic	Magnesium (umol/L) mean±SE	*p*
Age		<0.001
18-39 y	1.47±0.14	
40-59 y	1.47±0.13	
60-89 y	1.44±0.13	
Gender		<0.001
Male	1.52±0.14	
Female	1.43±0.13	
Marriage		0.113
Single	1.48±0.15	
Married	1.47±0.14	
Divorce	1.45±0.14	
Bereft of one's spouse	1.51±0.16	
Education		0.001
≤Elementary school	1.46±0.13	
Middle school	1.46±0.14	
High school	1.49±0.15	
College	1.48±0.15	
Postgraduate	1.51±0.12	
Income		<0.001
≤2000	1.44±0.126	
2001-4000	1.45±0.132	
4001-6000	1.46±0.134	
6001-8000	1.47±0.127	
≥8001	1.51±0.150	
Hearing loss family history		0.036
No	1.46±0.133	
Yes	1.47±0.141	
Hypertension‡		0.39
No	1.46±0.134	
Yes	1.46±0.135	
Smoking§		<0.001
Never	1.46±0.14	
Former	1.50±0.14	
Current	1.52±0.14	
Drinking¶		<0.001
Never	1.46±0.135	
Former	0.115±0.014	
Current	0.131±0.006	
Sleeping time		0.497
＜4 hours	1.47±0.117	
4-6 hours	1.45±0.130	
6-8 hours	1.46±0.133	
≥8 hours	1.46±0.138	
Living noise exposure		0.246
Never	1.46±0.135	
At least once a week	1.45±0.133	
At least once a day	1.47±0.135	
Occupational noise exposure		0.16
Never	1.46±0.134	
At least once a week	1.45±0.136	
At least once a day	1.46±0.128	

†Participants included individuals with all variables of interest: age, gender, marriage, education, income, hearing loss family history, Hypertension, smoking, drinking, sleeping time, living noise exposure and occupational noise exposure.
‡Current use of antihypertensive medication, systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg at the time of examination. § Smoked at least one cigarette per week as a current smoker. ¶ Drank at least once per week as an alcohol drinker. *p*: probability for statistic testing

Table 3. Multivariate-adjusted pure-tone average (95% CIs) of hearing thresholds by magnesium concentration quartile

Characteristic	Q1	Q2	Q3	Q4	*p* trend
Low-frequency					
Model 1†	0	-1.332	-0.439	-1.483	0.061
	(Reference)	(-2.467, -0.196)	(-1.562, 0.684)	(-2.648, -0.317)	
Model 2‡	0	-1.305	-0.378	-1.429	0.081
	(Reference)	(-2.450, -0.161)	(1.513, 0.757)	(-2.612, 0.246)	
Model 3§	0	-1.342	-0.247	-1.410	0.105
	(Reference)	(-2.480, -0.203)	(-1.377, 0.882)	(2.587, -0.232)	
Speech-frequency					
Model 1†	0	-0.873	0.039	-1.710	0.032
	(Reference)	(-2.012, 0.267)	(-1.088, 1.166)	(-2.881, -0.540)	
Model 2‡	0	-0.936	0.023	-1.849	0.022
	(Reference)	(-2.087, 0.216)	(-1.119, 1.164)	(-3.039, -0.659)	
Model 3§	0	-0.963	0.121	-1.886	0.022
	(Reference)	(-2.109, 0.183)	(-1.016, 1.258)	(-3.071, -0.701)	
High-frequency					
Model 1†	0	-1.289	0.030	-2.857	0.007
	(Reference)	(-2.794, 0.217)	(-1.465, 1.525)	(-4.435, -1.279)	
Model 2‡	0	-1.305	-0.011	-2.979	0.005
	(Reference)	(-2.827, 0.217)	(-1.523, 1.502)	(-4.574, -1.384)	
Model 3§	0	-1.394	0.136	-3.047	0.005
	(Reference)	(-2.912, 0.125)	(-1.374, 1.647)	(-4.640, -1.455)	

Q1 is the reference; Q, quartile (~25th percentile, ~median, ~75th percentile, ~100th percentile)
†Model 1: Adjusted for age, gender, marriage, education, income and hypertension (add gender at high-frequency)
‡Model 2: On the basis of model 1, additional adjustment for smoking, drinking and sleeping time
§Model 3: On the basis of model 2, adjusted for life noise expose and occupational noise expose
p: probability for statistic testing

Table 4. Multivariate-adjusted ORs (95%CIs) of hearing loss by magnesium concentration quartile

Characteristic	Q1	Q2	Q3	Q4	*p* trend
Low-frequency					
Model 1†	1 (Reference)	0.835 (0.655, 1.065)	0.960 (0.755, 1.221)	0.893 (0.695, 1.147)	0.617
Model 2‡	1 (Reference)	0.850 (0.664, 1.088)	0.976 (0.765, 1.246)	0.892 (0.691, 1.151)	0.624
Model 3§	1 (Reference)	0.844 (0.658, 1.082)	0.994 (0.777, 1.271)	0.899 (0.695, 1.163)	0.72
Speech-frequency					
Model 1†	1 (Reference)	0.987 (0.765,1.272)	1.185 (0.923,1.522)	0.839 (0.643,1.096)	0.527
Model 2‡	1 (Reference)	0.983 (0.760,1.272)	1.201 (0.932,1.547)	0.805 (0.614,1.056)	0.398
Model 3§	1 (Reference)	0.964 (0.743,1.251)	1.211 (0.937,1.565)	0.821 (0.624,1.079)	0.512
High-frequency					
Model 1†	1 (Reference)	0.744 (0.575,0.963)	0.789 (0.610,1.021)	0.450 (0.344,0.590)	<0.001
Model 2‡	1 (Reference)	0.758 (0.584,0.984)	0.793 (0.611,1.030)	0.440 (0.335,0.579)	<0.001
Model 3§	1 (Reference)	0.762 (0.586,0.991)	0.821 (0.631,1.069)	0.446 (0.339,0.587)	<0.001

Q1 is the reference; Q, quartile (~25th percentile, ~median, ~75th percentile, ~100th percentile)
†Model 1: Adjusted for age, gender, marriage, education, income and hypertension (add gender at high-frequency)
‡Model 2: On the basis of model 1, additional adjustment for smoking, drinking and sleeping time
§Model 3: On the basis of model 2, adjusted for life noise expose and occupational noise expose
p: probability for statistic testing