Association of Dyslipidemia With Sudden Sensorineural Hearing Loss: A Retrospective Study

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Research

Keywords: Sudden sensorineural hearing loss (SSNHL), Dyslipidemia, LDL-C, apo AI, apo B, The optimum cutoff values

Posted Date: February 11th, 2020

DOI: https://doi.org/10.21203/rs.2.23151/v1

Abstract

Background: Blood lipid levels have been widely studied in patients with sudden sensorineural hearing loss (SSNHL), but it has been unclear whether dyslipidemia associates with SSNHL. Whether there is a simple and feasible blood lipid index to predict the onset of SSNHL remains to be found.

Methods: This study reviewed 100 SSNHL patients and 100 healthy subjects who received relevant clinical examination in our hospital from June 1, 2015 to June 1, 2019. The demographic, clinical characteristics, lipid levels and lipid metabolism indexes of the two groups were compared.

Results: In this study, 100 patients (64 men [64%]; 36 women [36%]; mean [SD] age, 38.47 [14.36] years) were included in the SSNHL group, and 100 healthy people(60 men [60%]; 40 women [40%]; mean [SD] age, 36.52 [9.86] years) served as the control group. No significant differences between the SSNHL group and the control group in age, sex, BMI, smoking habits and alcohol drinking patterns were observed. Meanwhile, it can be seen the mean (SD) concentrations of total cholesterol (TC) (194.59 [38.22] vs 176.83 [23.55] mg/dL; MD, 17.76 mg/dL; 95% CI, 26.64-46.72 mg/dL), the mean (SD) concentrations of low density lipoprotein cholesterol (LDL-C) (116.99 [33.59] vs 96.91 [22.01] mg/dL; MD, 20.08 mg/dL; 95% CI, 32.43-48.26 mg/dL) and apolipoprotein (apo) B (89.82 [21.38] vs 81.16 [16.17] mg/dL; MD, 8.66 mg/dL; 95% CI, 12.03-23.21 mg/dL) were significantly higher than the control group. In addition, it was also observed that the median [IQR] concentrations of high density lipoprotein cholesterol (HDL-C) (1.51 [1.33-1.76] vs 1.56 [1.40-1.84] mg/dL) and the median [IQR] concentrations of apolipoprotein (apo) AI (118.50 [103.00-141.25] vs 133.00 [115.25-1.52.75] mg/dL) were lower than those in the control group. In terms of lipid metabolism indexes, the median [IQR] value of TC/HDL-C (3.31 [2.68-3.85] vs 2.72 [2.42-3.37]), the mean (SD) value of apo B/apo AI (0.76 [0.26] vs 0.63 [0.18]; MD, 0.13; 95% CI, 0.20-0.32) and the median [IQR] value of atherogenic index (ATH index) (1.61 [0.97-2.50] vs 1.01 [0.73-1.75]) were significantly higher than the control group, while the mean (SD) value of atherogenic index of plasma (AIP) (-0.24 [0.28] vs -0.25 [0.21]; MD, 0.01; 95% CI, -0.06-0.08) showed no difference between the two groups.

Conclusions: There were significant differences in blood lipid levels and lipid metabolism between the SSNHL group and the control group. LDL-C, apo AI and apo B were important independent predictors of SSNHL.

Background

Sudden sensorineural hearing loss (SSNHL) is defined as sensorineural hearing loss of more than 30 dB over three consecutive pure tone frequencies occurring within 72 hours[1]. SSNHL affects between 5 and 27 people per 100,000 people annually, with about 66,000 new cases annually in the United States[1]. It can be seen that the incidence of SSNHL has gradually increased in recent years. However, the etiology and pathogenesis of SSNHL are still unclear. Current studies suggest that viral infections[2], autoimmune diseases[3], inflammatory lesions, tumors[5], trauma[6] and vascular diseases[7] are associated with

SSNHL. In addition, the currently more recognized possible pathogenesis of SSNHL focuses on the inner ear vascular spasm, vascular striatum dysfunction, vascular embolism or thrombosis, hydrocephalus membranous labyrinth and hair cell damage. Among them, more and more evidence points to a tight relationship between dyslipidemia and SSNHL[7]. Dyslipidemia will lead to thrombosis and atherosclerosis, affect the blood supply of cochlea hair cells, and eventually lead to the onset of SSNHL[12].

Obviously, dyslipidemia associates with hearing loss. But the problem now is that some studies do not support dyslipidemia affecting SSNHL[13]. Therefore, the purpose of this study was to evaluate the differences of lipid levels and lipid metabolism between the SSNHL group and the control group, and find out the risk factors of SSNHL under the condition of eliminating hypertension, diabetes, coronary heart disease and other interfering factors that may affect blood lipid.

Methods

Patients and controls

We reviewed 100 SSNHL patients and 100 healthy subjects who received relevant clinical examination in The third affiliated hospital of southern medical university from June 1, 2015 to June 1, 2019. SSNHL is defined as sensorineural hearing loss of more than 30 dB over three consecutive pure tone frequencies occurring within 72 hours. We classified SSNHL patients as the SSNHL group, and healthy subjects as the control group. The inclusion criteria for the SSNHL group were as follows: (1) SSNHL of more than 30 dB appearing on at least three consecutive frequencies within 72 hours; (2) the patient was admitted to hospital within 7 days after onset; (3) magnetic resonance imaging (MRI) excluded intracranial tumors and other lesions; (4) age ≥ 14 years; (5) No history of neurological disease, infectious disease, mental disease, craniocerebral injury, ear surgery, noise-induced hearing loss or meniere's disease or ototoxic drugs; and (6) absence of chronic diseases such as hypertension, diabetes, coronary heart disease and otitis media.

The control group was made up of people from different communities who came from our hospital for physical examination. The inclusion criteria for the control group were as follows: (1) the participants had normal bilateral hearing; (2) no history of hearing loss or autoimmune or metabolic diseases, and no history of hypertension, diabetes, coronary heart disease, otitis media, etc; (3) age ≥ 14 years. Participants in both groups had a negative history of familial deafness.

Ethical Considerations

The study protocol was in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the Institutional Review Board at The third affiliated hospital of southern medical university. All patients were given informed consent.

Audiometric Evaluation

All hearing was evaluated by pure tone audiometry using the Denmark AD229B diagnostic audiometer by the same speech and hearing therapist in the same audiology laboratory. Acoustic immittance examination was performed by Denmark AT235 acoustic impedance instrument to exclude middle ear lesions. And posterior cochlear lesions were excluded by auditory brainstem response (ABR) through the International EClipse hearing objective detection system. All patients underwent computed tomography (CT) or MRI scans to exclude structural abnormalities in the inner ear or intracranial tumors.

Lipid measurements

Blood samples from both the SSNHL group and the control group were taken between 6 a.m. and 8 a.m. after overnight fasting. The blood samples were sent to the laboratory department of the hospital for testing, including the values of TC, TG, LDL, HDL, apo AI and apo B. Subsequently, clinical indicators of lipid metabolism, including TC/HDL-C, apo B/apo AI, AIP and ATH index were calculated. Using the logarithm of the ratio of the molar concentration (mmol/L) of TG to HDL-C to represent the value of AIP(i.e., log [TG/HDL-C])[13]. The ATH index was calculated by the following equation: ATH index = ((TC – HDL-C) * apoB) / (HDL-C * apoA-I)[15, 16].

Statistical Analysis

When the variables are normal distribution, they were expressed as mean ± SD and compared by Student's two-tail test. For variables that were not normally distributed, they were expressed as the median and interquartile range (25th and 75th percentiles) and compared by the Mann-Whitney test. Categorical data were presented as frequencies or proportion and tested by chi-square test. Receiver operating characteristic (ROC) curves were plotted to determine the optimum cutoff points. The area under curve (AUC) was used as an estimation of diagnostic accuracy. Univariate and multivariate logistic regression analysis was used to evaluate the effect of serum lipid levels and lipid metabolism indexes on SSNHL, and odds intervals with their 95% confidence intervals were calculated. Statistical analysis was performed by using SPSS 25.0 software (SPSS, Chicago, IL). $P < .05$ was defined as statistically significant.

Results

The characteristics of participants in the SSNHL group and the control group can be seen in Table 1. No significant differences between SSNHL group and control group in age, sex, BMI, smoking habits and alcohol drinking patterns were observed. Meanwhile, it can be seen that the adverse indicators for vascular circulation: the mean (SD) concentrations of TC (194.59 [38.22] vs 176.83 [23.55] mg/dL; MD, 17.76 mg/dL; 95% CI, 26.64–46.72 mg/dL), the mean (SD) concentrations of LDL (116.99 [33.59] vs 96.91 [22.01] mg/dL; MD, 20.08 mg/dL; 95% CI, 32.43–48.26 mg/dL) and apoB (89.82 [21.38] vs 81.16 [16.17] mg/dL; MD, 8.66 mg/dL; 95% CI, 12.03–23.21 mg/dL) were significantly higher than the control group. In addition, it was also observed that the median [IQR] concentrations of HDL (1.51 [1.33–1.76] vs 1.56 [1.40–1.84] mg/dL) and the median [IQR] concentrations of apo A (118.50 [103.00-141.25] vs 133.00 [115.25–1.52.75] mg/dL) were lower than those in the control group. In terms of lipid metabolism

indexes, the median [IQR] value of TCTC/HDL (3.31 [2.68–3.85] vs 2.72 [2.42–3.37]), the mean (SD) value of apo B/apo AI (0.76 [0.26] vs 0.63 [0.18]; MD, 0.13; 95% CI, 0.20–0.32) and the median [IQR] value of ATH index (1.61 [0.97–2.50] vs 1.01 [0.73–1.75]) were significantly higher than the control group, while the mean (SD) value of AIP (-0.24 [0.28] vs -0.25 [0.21]; MD, 0.01; 95% CI, -0.06-0.08) showed no difference between the two groups (Table 1).

TABLE 1.

Demographic and clinical characteristics of participants in both groups.

Characteristic	SSNHL group	control group	Effect Size (95% CI)
	n = 100	n = 100	
Age, mean (SD), y	38.47(14.36)	36.52 (9.86)	1.95 (-1.49 to 5.38)
Sex No.(%)			
Male	64(64)	60(60)	4.00 (-9.32 to 17.12)
Female	36(36)	40(40)	-4.00 (-17.12 to 9.32)
Smoking, NO. (%)	29(29)	22(22)	7.00 (-5.08 to 18.83)
Alcohol drinking patterns, NO. (%)	17(17)	11(11)	6.00 (-3.77 to 15.78)
BMI, midian (IQR)	22.33 (19.75; 24.66)	21.54 (20.46; 23.93)	NA
Lipid levels (mg/dL):			
TC, mean (SD)	194.59 (38.22)	176.83 (23.55)	17.76 (26.64 to 44.02)
TG, midian (IQR)	31.66 (22.01 to 47.10)	35.91(26.64 to 46.72)	NA
HDL-C, midian (IQR)	58.30(51.35 to 67.95)	60.23 (54.05 to 71.04)	NA
LDL-C, mean (SD)	116.99 (33.59)	96.91 (22.01)	20.08 (32.43 to 48.26)
apo AI, midian (IQR)	118.50 (103.00 to 141.25)	133.00 (115.25 to 152.75)	NA
apo B, mean (SD)	89.82 (21.38)	81.16 (16.17)	8.66 (12.03 to 23.21)
Indicators of lipid metabolism:			
TC/HDL-C, midian(IQR)	3.31 (2.68 to 3.85)	2.72 (2.42 to 3.37)	NA
apo B/apo AI, mean (SD)	0.76 (0.26)	0.63 (0.18)	0.13 (0.20 to 0.32)
AIP, mean (SD)	-0.24 (0.28)	-0.25 (0.21)	0.01 (-0.06 to 0.08)
ATH index, midian(IQR)	1.61(0.97 to 2.50)	1.01(0.73 to 1.75)	NA
SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259. [1]Indicates mean difference for continuous variables and percentage difference for categorical variables.			
p-values < 0.05 are shown in boldface type			

We selected statistically significant indicators from Table 1 to draw the ROC curves. Therefore, the ROC curves for SSNHL were plotted to determine the optimum cutoff values for the TC (> 201.54 mg/dL); HDL (≤ 52.51 mg/dL); LDL (> 106.56 mg/dL); apo AI (≤ 127.13 mg/dL); apo B (> 106.33 mg/dL); TC/HDL-C (> 2.85); apo B/apo AI (> 0.81) and ATH index (> 1.23) (Table 2). (TC: AUC, 0.634; p = 0.001; 95% CI, 0.557 to 0.711; HDL-C: AUC, 0.583; P = 0.004; 95% CI, 0.505 to 0.662; LDL-C: AUC, 0.687; p < 0.001; 95% CI, 0.614 to 0.761; apo AI: AUC, 0.626; p = 0.001; 95% CI, 0.548 to 0.703; apo B: AUC, 0.604; p = 0.01; 95% CI, 0.525 to 0.682; TC/HDL-C: AUC, 0.671; p < 0.001; 95% CI, 0.598 to 0.745; apo B/apo AI: AUC, 0.649; p < 0.001; 95% CI, 0.574 to 0.725; ATH index: AUC, 0.664; p < 0.001; 95% CI, 0.590 to 0.739).

TABLE 2.

The optimum cutoff values were used to describe the characteristics of two groups.

Variants	SSNHL group, NO.(%)	Control group, NO.(%)	Effect Size
	n = 100	n = 100	(95% CI)
TC > 201.54 (mg/dL)	39(39)	17(17)	22.0 (9.6 to 33.5)
HDL-C ≤ 52.51 (mg/dL)	32(32)	19(19)	13.0 (9.0 to 24.6)
LDL-C > 106.56 (mg/dL)	65(65)	36(36)	29.0 (15.2 to 41.3)
apo AI ≤ 127.13 (mg/dL)	60(60)	38(38)	22.0 (8.2 to 34.7)
Apo B > 106.33 (mg/dL)	25(25)	4(4)	21.0 (11.5 to 30.6)
TC/HDL-C > 2.85	67(67)	44(44)	23.0 (9.2 to 35.6)
apo B/apo AI > 0.81	37(37)	13(13)	24.0 (12.1 to 35.1)
ATH index > 1.23	66(66)	47(47)	19.0 (5.3 to 31.8)
SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259. [1]Indicates percentage difference for categorical variables.			
Then, logistic regression analysis was used to evaluate the pathogenesis of SSNHL. Through univariate regression analysis, we found that TC > 201.54 mg/dL (OR, 3.12; p = 0.001; 95% CI, 1.62–6.03); HDL-C ≤ 52.51 mg/dL (OR, 2.01; p = 0.04; 95% CI, 1.04–3.85); LDL-C > 106.56 mg/dL (OR, 3.45; p = < 0.001; 95% CI, 1.93–6.17); apo AI ≤ 127.13 mg/dL (OR, 2.45; p = 0.002; 95% CI, 1.39–4.32); apoB > 106.33 mg/dL (OR, 8.00; p < 0.001; 95% CI, 2.67–23.98); TC/HDL-C > 2.85 (OR, 2.58; p = 0.001; 95% CI, 1.46–4.59); apo B/apo AI > 0.81 (OR, 3.93; p < 0.001; 95% CI, 1.93-8.00) and ATH index > 1.23 (OR, 2.19; p = 0.007; 95% CI, 1.24–3.89) were considered as risk factors for SSNHL. After that, through multivariate regression analysis, only LDL-C > 106.56 mg/dL (OR, 2.64; p = 0.003; 95% CI, 1.40–4.99); apo AI ≤ 127.13 mg/dL (OR, 2.49; p = 0.004; 95% CI, 1.35–4.59) and apoB > 106.33 mg/dL (OR, 4.63; p = 0.01; 95% CI, 1.44–14.83) were truly considered as independent predictors of SSNHL (Table 3). Individuanls with higher LDL-C, apo B and lower apo AI had a 2.64-fold, 2.49-fold and 4.63-fold higher risk of SSNHL than healthy people.			

TABLE 3.

Univariate and multivariate logistic regression analysis of prediction for SSNHL (n = 200).

Variables		Univariate			Multivariate	
	OR	95% CI	p value	OR	95% CI	p value
TC > 201.54 (mg/dL)	3.12	1.62–6.03	0.001			
HDL-C ≤ 52.51 (mg/dL)	2.01	1.04–3.85	0.04			
LDL-C > 106.56 (mg/dL)	3.45	1.93–6.17	< 0.001	2.64	1.40–4.99	0.003
apoAI ≤ 127.13 (mg/dL)	2.45	1.39–4.32	0.002	2.49	1.35–4.59	0.004
apoB > 106.33 (mg/dL)	8.00	2.67–23.98	< 0.001	4.63	1.44–14.83	0.01
TC/HDL-C > 2.85	2.58	1.46–4.59	0.001			
apo B/apo AI > 0.81	3.93	1.93-8.00	< 0.001			
ATH index > 1.23	2.19	1.24–3.89	0.007			
SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259.						
p-values < 0.05 are shown in boldface type						

Discussion

SSNHL, as a common emergency in otolaryngology, its etiology is complex and varied, which is still unknown. Many studies had linked lipid levels to hearing, but the jury is still out. In order to reflect the blood lipid levels of patients with SSNHL as truly as possible, we excluded hypertension, diabetes, coronary heart disease and other factors that might affect lipid profile from the two groups to explore the difference in lipid profile between the sudden deafness group and the control group. Through our study, it can be obeserved that dyslipidemia affected SSNHL. We found that the mean value or median value of lipid levels and lipid metabolism indexes in the two groups were almost within the normal range. However, the TC, LDL-C, apo B, TC/HDL-C, apo B/apo AI and ATH index in the SSNHL group were significantly higher than those in the control group, while the HDL-C and apo AI were lower. This result is basically consistent with other studies[8, 17, 18]. Different from the result of other study, there was no significant difference between the two groups in AIP[10]. In addition, although apo B/aoo AI and ATH index were higher in the SSNHL group than in the control group, but multivariate regression analysis denied that they were independent risk factors for SSNHL. Of course, more research is needed to confirm this conclusion.

The effect of lipids on hearing is mainly reflected in the inner ear circulation. The blood supply to the inner ear is closely related to the labyrinth artery. Dyslipidemia can lead to the increase of lipids and cholesterol in the inner wall of blood vessels, thus affecting the blood oxygen supply in the inner ear.

Studies have also found that insufficient blood supply from the basilar artery is associated with SSNHL. LDL-C is a lipoprotein particle that carries cholesterol into peripheral tissue cells and can be oxidized to oxidized LDL-C (ox-LDL-C). When LDL, especially ox-LDL-C, is excessive, the cholesterol it carries accumulates in the walls of the arteries, gradually hardening the arteries[20]. As cardiovascular risk factors, LDL-C and TC are closely related to thrombosis, and have a significant impact on the occurrence of SSNHL[20]. Apo AI is mainly synthesized by the liver and is the main structural protein of HDL-C, accounting for 60% ~ 70% of the HDL-C. A decrease in apo AI means a decrease in the ability of HDL-C protein to export cholesterol and promote cholesterol metabolism. In addition, apo B is present on the surface of LDL-C lipoprotein, so cells can recognize and ingestion LDL-C by recognizing apo B. Our data supported that higher LDL, apo B and lower apo AI were closely related to SSNHL, which was consistent with the theory.

Similar to other studies, we also found that compared with the control group, the TC/HDL ratio, apo B/apo AI ratio and ATH index in SSNHL were higher[10], suggesting the possibility of atherosclerosis in SSNHL patients[21, 23]. Apo B/apo AI ratio and ATH index were also found to be favorable predictors of plasma atherosclerosis[15, 24]. This prompts that in studying the relationship between dyslipidemia and SSNHL, we should not only evaluate the conventional lipid indices, but also evaluate atherogenicity in detail.

Moreover, through the ROC curves for SSNH,we determined the optimum cutoff values for TC (> 201.54 mg/dL); HDL-C (≤ 52.51 mg/dL); LDL-C (> 106.56 mg/dL); apo AI (≤ 127.13 mg/dL); apo B (> 106.33 mg/dL); TC/HDL-C (> 2.85); apo B/apo AI (> 0.81) and ATH index (> 1.23). And, multivariate regression analysis suggested only LDL-C, apo AI and apo B were truly considered as independent predictors of SSNH. Therefore, we strongly speculated that dyslipidemia is involved in the pathogenesis of SSNHL. Correcting dyslipidemia can improve the prognosis of SSNHL and avoid the onset of secondary bilateral SSNHL[25, 26].

One of the major limitations is that our study is a retrospective study with data from a single institution. This requires new, advanced, randomized, controlled trials to further support our results.

Conclusions

There were significant differences in serum lipid levels and lipid metabolism between the SSNHL group and the control group. LDL-C, apo AI and apo B were important independent predictors of SSNHL.

Abbreviations

NA, not applicable; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; apo AI, apolipoprotein AI; apo B, apolipoprotein B; AIP, atherogenic index of plasma; ATH index, atherogenic index; SSNHL, sudden sensorineural hearing loss.

Declarations

Acknowledgements

Not applicable.

Finding

This work was supported by grants from the Guangdong Science and Technology Innovation Project (no.2018A070706003; H. L.).

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Dafei Li and Guangyong Tian had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Dafei Li and Guangyong Tian. Acquisition, analysis, or interpretation of data: Dafei Li, Jiawei Chen, Qiongping Lin and Haiyan Zhao. Drafting of the manuscript: Dafei Li. Critical revision of the manuscript for important intellectual content: Dafei Li and Guangyong Tian. Statistical analysis: Dafei Li, Piao Xu. Obtained funding: Guangyong Tian. Administrative, technical, or material support: Guangyong Tian and Jingya Yang. Study supervision: Guangyong Tian.

Authors' information

Not applicable.

Ethics approval and consent to participate

This study protocol was in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the Institutional Review Board at The third affiliated hospital of southern medical university. All patients were given informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

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