The Journal of International Advanced Otology

J Int Adv Otol 2023; 19(4): 277–282 • DOI: 10.5152/iao.2023.22991

Review

Sensorineural Hearing Loss in Autoimmune Diseases: A Systematic Review and Meta-analysis

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Cite this article as: Li X, Cao Z, Chen F, Yang D, Zhao F. Sensorineural hearing loss in autoimmune diseases: A systematic review and meta-analysis . *J Int Adv Otol.* 2023;19(4):277-282.

Autoimmune diseases may cause various kinds of conflicts in and outside the target organ, and some evidence brings forward the suggestion that autoimmune diseases may damage the auditory nerve and cause sensorineural hearing loss. However, this relationship is not clearly defined yet. Therefore, the aim of this study was to assess sensorineural hearing loss in autoimmune diseases through systematic review and meta-analysis. The literature databases of PubMed, Google Scholar, Scopus, Web of knowledge, and Cochrane library were thoroughly searched, and a meta-analysis study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Eighteen articles were included, involving 27 859 cases affected by autoimmune diseases. The prevalence of sensorineural hearing loss in systemic lupus erythematosus cases was 21.26 [3.80, 38.71]%, which was significant, and pooled analysis of odds ratio observed in individual studies showed that the odds of sensorineural hearing loss prevalence was 12.11 [7.4, 24.12] ($P < .001$). The prevalence of sensorineural hearing loss in rheumatoid arthritis cases was 16.14 [–9.03, 41.31]%, which was significant, and pooled analysis of odds ratio observed in individual studies showed that the odds of sensorineural hearing loss prevalence was 2.23 [1.84, 2.32] ($P < .001$). In vitiligo cases, the prevalence of sensorineural hearing loss was 38.80 [22.36, 55.25]%, which was significant, and pooled analysis of odds ratio observed in individual studies showed that the odds of sensorineural hearing loss prevalence was 5.82 [3.74, 9.68] ($P < .001$). The present study showed that sensorineural hearing loss is significantly related to the autoimmune diseases of systemic lupus erythematosus, rheumatoid arthritis, and vitiligo. Therefore, these cases need a routine evaluation of sensorineural hearing loss.

KEYWORDS: Hearing Loss, Sensorineural Hearing Loss (SNHL), Sudden Hearing Los, Autoimmune Diseases

INTRODUCTION

Sensorineural hearing loss (SNHL) is characterized by increased bone conduction thresholds. The etiology of SNHL is complex, which may be caused by congenital and acquired factors. Cases with congenital hearing loss are presented with hearing deficits since birth or since the early periods of life, while acquired hearing loss can be due to noise exposure, infection, ototoxic drugs, neoplasm, and aging. Acquired SNHL may also be "idiopathic," which is called sudden sensorineural hearing loss (SSNHL). Sensorineural hearing loss is a relatively frequent condition in Otology and Audiology clinics.[1-3] Despite extensive research, regardless of the cause, the etiologies of SSNHL and the appropriate care that should be delivered to cases with idiopathic SSNHL are still subjects of great controversy.[4-6] The restoration of hearing thresholds after SSNHL varies for different cases. It is affected by factors such as the age of the case at the beginning of hearing loss, the severity and frequency of hearing loss, the presence of vertigo, and the time interval between the onset of hearing loss and the clinical consultation.[7-10]

A great number of clinical and experimental trials have revealed that autoimmune diseases may play a crucial role in the pathophysiology of SNHL or SSNHL, but the lack of documentation represents an important problem in this theory. These studies reveal that SNHL or SSNHL is associated with other autoimmune diseases, or symptoms of major systemic autoimmune diseases, such as autoimmune hepatitis, sympathetic hyperalgesia, edema syndrome, Cogan's syndrome, systemic lupus erythematosus

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Received: December 02, 2022 • **Accepted:** February 12, 2023 • **Publication Date:** July 31, 2023
Available online at www.advancedotology.org

(SLE), multiple sclerosis, nodular rheumatoid arthritis, and Crohn's disease.[11-14]

The pathophysiology behind the inner ear in systemic autoimmune diseases remains imprecise. Complement system activation, cell-mediated cytotoxicity blockade, direct role of cytotoxic T cells, or damage mediated by the immune complex may be elicited.[15,16] In addition, tinnitus observed in systemic autoimmune diseases is mostly associated with hearing loss. In the past, it has been shown that a decline in peripheral input after a hearing loss can lead to a neuroplasticity response. As a result, a peripheral hearing impairment may elicit central changes, which finally can cause tinnitus in cases who are living with autoimmune diseases.

Furthermore, autoimmune diseases may cause various complications at the target organ, and some evidence suggests that autoimmune diseases, for example, rheumatoid arthritis (RA), systemic SLE, and vitiligo, may damage the sensorineural nerves and cause sensorineural hearing loss. However, the exact connection between vitiligo and SNHL is not clearly defined. For example, SNHL is the most frequently encountered audiovestibular symptom in cases with SLE, with an incidence of 6%-70%. Sensorineural hearing loss is the most commonly encountered type of hearing impairment in RA cases, with a prevalence of 25%-72%, while the prevalence is 7.69% for vitiligo. Unfortunately, as mentioned above, this epidemiological report was not able to describe the exact connection between SNHL and this group of autoimmune diseases, and the basic pathological links remain to be further documented.

Because there is no available research analyzing the definite relationship between a group of autoimmune diseases and SNHL, this study aimed to evaluate SNHL in autoimmune diseases through systematic review and meta-analysis.

METHODS

Search Method

This study conformed to the Systematic Reviews and Meta-Analyses (PRISMA) statement. The Scopus, PubMed, ISI, Google Scholar, and Cochrane library databases were used to search related articles between 2011 and December 2021. Also, EndNote was used for the management of electronic resources, and PubMed searching was conducted using the following mesh terms: ("Sudden Hearing Loss/ Autoimmune Diseases" [Mesh] OR "Sudden Hearing Loss/systemic lupus erythematosus"[Mesh] OR "Sudden Hearing Loss/rheumatoid arthritis"[Mesh])) OR ("Sudden Hearing Loss/ vitiligo "[Mesh])) OR ("Sudden Hearing Loss/Inflammatory bowel disease"[Mesh])) OR ("Sudden Hearing Loss/Multiple sclerosis"[Mesh])) AND "Sensorineural hearing loss, Autoimmune Diseases" [Mesh])). For the remaining databases, these keywords were used: sensorineural hearing loss, sudden hearing loss, autoimmune diseases, systemic lupus erythematosus, rheumatoid arthritis, vitiligo, inflammatory bowel disease, and multiple sclerosis. In addition, manual retrieval was performed for the relevant references from the selected publications, as well as the abstracts from scientific meetings over the last 5 years.

Inclusion and Exclusion Criteria

Inclusion criteria: controlled clinical trials, randomized controlled trials, and prospective and retrospective cohort studies. Case studies, in vitro studies, reviews, and case reports were excluded from this present article.

Data Extraction and data statistical analysis

Two authors (LX and ZC) examined the titles and abstracts of the articles independently to verify the relevance. After reviewing the full texts, according to the inclusion and exclusion criteria, relevant studies were identified and included as suitable studies. When disagreements arose and could not be resolved through discussion, arbitration by 1 of the other authors (FC, DY, FZ) was solicited. Two authors (LX and ZC) conducted data extraction from the studies by using an agreed data collection form independently. The extracted data included information such as study design, sample size, mean age, stage, follow-up, and treatment duration. Hazard ratio, odds ratio, and risk ratio with 95% CI, fixed and Mantel-Haenszel methods were calculated. The extracted data were double-checked for accuracy, and any divisions in the opinion that could not be solved through discussion were arbitrated by one of the other authors (DY, FZ). Subgroup analysis was performed according to the type of disease. The statistical software of Stata 16.0 (StataCorp, Texsa, USA) was used for evaluation in this meta-analysis.

RESULTS

Finally, 18 articles[17-33] were included in the study (Figure 1 presents the selection process of the studies in a PRISMA flow diagram), in which 7 articles examined the prevalence of SNHL in SLE cases (there was 1 article from Brazil, 1 article from Korea, 1 article from Spain, 1 article from Iran, 1 article from Egypt, 1 article from the United States, and 1 article from Poland), 5 articles examined the prevalence of SNHL in RA cases (there was 1 article from Korea, 1 article from Taiwan, 1 article from Mexico, 1 article from Iran, and 1 article from Brazil), and 6 articles examined the prevalence of SNHL in vitiligo cases (there were 2 articles from Egypt, 1 article from Israel, 1 article from India, and 2 articles from Turkey). Characteristics of the studies are displayed in Tables 1-3.

Meta-analysis and Subgroup Analysis Results

The results of a review of 7 articles related to the prevalence of SNHL in SLE cases showed that a wide range of prevalence was reported in different articles, varying from 0.6% to 70%. Also, the sample sizes varied from 20 to 7168. These articles revealed that the prevalence of SNHL in SLE cases was 21.26 [3.80, 38.71]%, which was statistically significant, and pooled analysis of ORs observed in individual studies showed that the odds of SNHL prevalence was 12.11 [7.4, 24.12] ($P < .001$) (Figure 2).

The results of a review of 5 articles related to the prevalence of SNHL in RA cases showed that a wide range of prevalence was reported in different articles, which varied from 0.38% to 46.5%. Moreover, the sample sizes varied from 42 to 18 267. These articles revealed that the prevalence of SNHL in RA cases was 16.14 [−9.03, 41.31]%, which was statistically significant, and pooled analysis of ORs observed in individual studies showed that the odds of SNHL prevalence was 2.23 [1.84, 2.32] ($P < .001$) (Figure 3).

The results of a review of 6 articles related to the prevalence of SNHL in vitiligo cases showed that a wide range of prevalence was reported in different articles, which varied from 22.37% to 68.8%. Also, the sample sizes varied from 16 to 143. These articles revealed that the prevalence of SNHL among vitiligo cases was 38.80 [22.36,

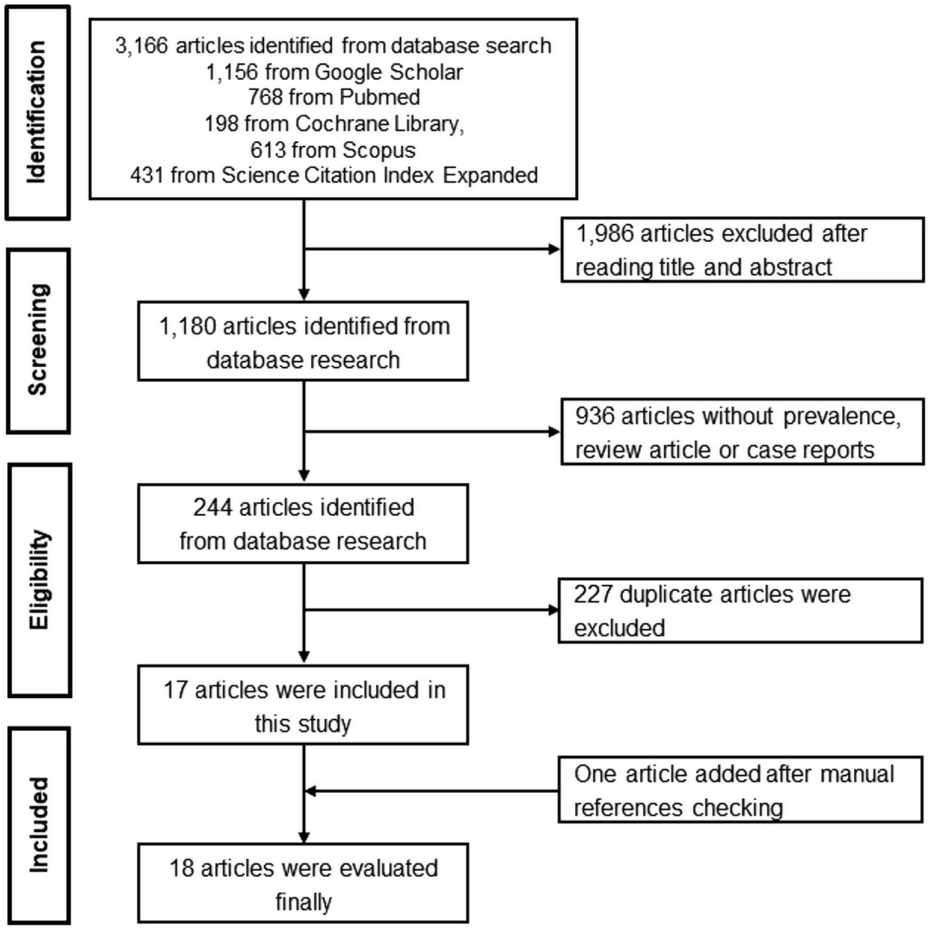

Figure 1 . Flowchart of the study selection process. 18 articles were ultimately included in this study.

Table 1. Characteristics of the Included Studies Concerning the Prevalence of SNHL in SLE Cases

Reference	Author	Year	Country	Study Design	N	Age	Female Gender	Prevalence of SSNHL
17	Polanski et al	2020	Brazil	Cross-sectional	43	40.8	97.6	23.2
18	Jeong et al	2019	Korea	Cohort	229	>20	66.65	1.74
19	Lasso de la Vega	2017	Spain	descriptive cross-sectional	55	46	71.3	70
20	Abbasi et al	2013	Iran	Case–control	45	34.9	91.1	11.11
21	Gad et al	2013	Egypt	Case–control	20	12.9	85	25
22	Lin et al	2013	USA	Cohort	7168	35.71	88	0.6
23	Maciaszczyk et al	2011	Poland	descriptive	35	47.8	94.28	17.1

SLE, systemic lupus erythematosus; SNHL, sensorineural hearing loss.

Table 2. Characteristics of the Included Studies Concerning the Prevalence of SNHL in RA Cases

Reference	Author	Year	Country	Study Design	N	Age	Female Gender	Prevalence of SSNHL
18	Jeong et al	2019	Korea	Cohort	13 250	≥20 years	66.65	1.09
24	Huang et al	2018	Taiwan	Cohort	18 267	53.6	78	0.38
25	Galarza-Delgado et al	2017	Mexico	Cross-sectional	117	47.5	100	66.7
26	Ahmadzadeh et al	2017	Iran	Cross-sectional	42	53	91	11.9
27	Lobo et al	2016	Brazil	Cross-sectional	43	48.86	86	46.5

RA, rheumatoid arthritis; SNHL, sensorineural hearing loss.

Table 3. Characteristics of the Included Studies Concerning the Prevalence of SNHL in Vitiligo Cases

Reference	Author	Year	Country	Study Design	N	Age	Female Gender	Prevalence of SSNHL
28	Mohamed et al	2017	Egypt	Case–control	40	29.33	74	37.5
29	Maheshwari et al	2016	Egypt	Case–control	50	<80	60	54.55
30	Fleissig et al	2013	Israel	Case–control	16	32.72	50	68.8
31	Al-Mutairi et al	2011	India	Case–control	143	>40	52.7	22.37
32	Akay et al	2010	Turkey	Case–control	53	37	62.5	37.7
33	Aslan et al	2010	Turkey	Case–control	22	33.13	60	36.4

SNHL, sensorineural hearing loss.

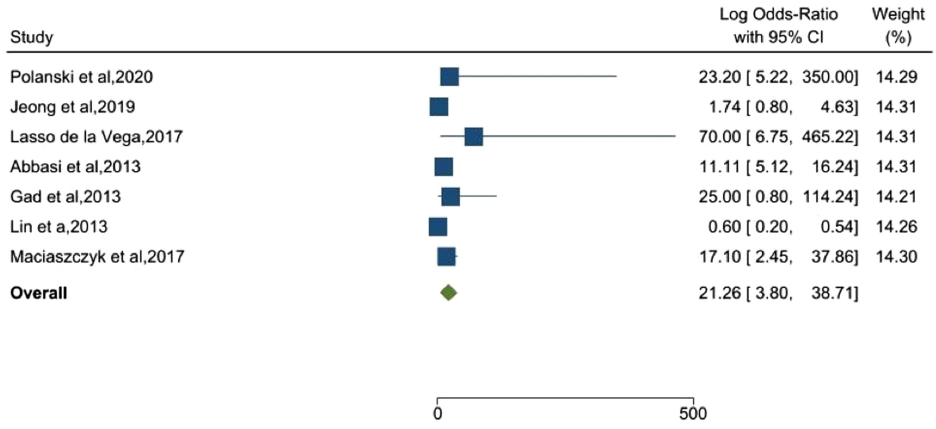

Figure 2. Forest plot of the prevalence of SNHL in SLE cases. The prevalence of SNHL in SLE cases was 21.26 [3.80, 38.71]%, which was statistically significant. SLE, systemic lupus erythematosus; SNHL, sensorineural hearing loss.

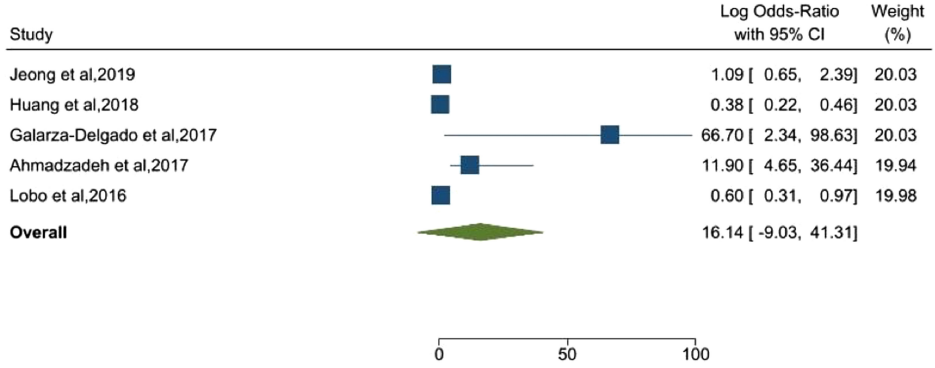

Figure 3. Forest plot of the prevalence of SNHL in RA cases. The prevalence of SNHL in RA cases was 16.14 [−9.03, 41.31]%, which was statistically significant. RA, rheumatoid arthritis; SNHL, sensorineural hearing loss.

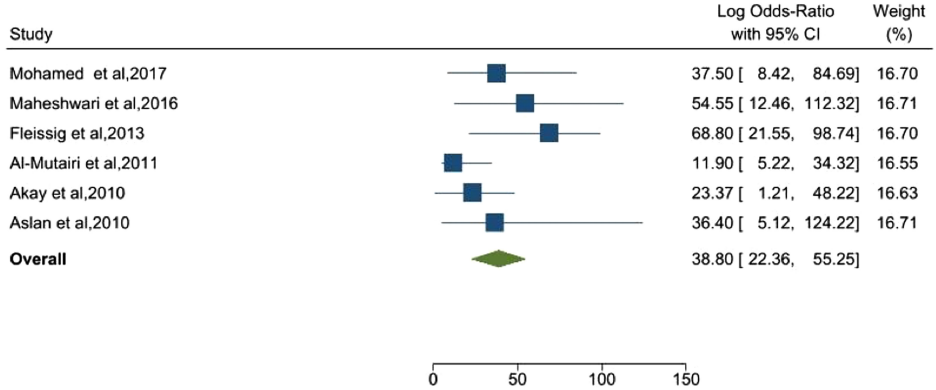

Figure 4. Forest plot of the prevalence of SNHL in vitiligo cases. The prevalence of SNHL in vitiligo cases was 38.80 [22.36, 55.25]%, which was statistically significant. SNHL, sensorineural hearing loss.

55.25]%, which was statistically significant, and pooled analysis of ORs observed in individual studies showed that the odds of SNHL prevalence was 5.82 [3.74, 9.68] ($P < .001$) (Figure 4). Also, other hearing related variables, such as hearing frequencies, were not investigated in the different studies to show a significant difference. As for other demographic variables such as weight, height, and body mass index, no statistical analysis was performed.

DISCUSSION

Unlike other forms of SNHL, such as age-related hearing loss and noise-induced hearing loss, which have recognized causes, most cases with SSNHL have unknown etiologies. Therefore, more studies have been done to investigatethe causes of SSNHL and the factors related to this disease.[34-36] Of these, some studies found a significant relationship between SSNHL and autoimmune diseases. The immune hypothesis is established on the idea that distributed antibodies activate certain cells or interact with inner ear antigens to destroy the inner ear. These antibodies may be caused by viruses or other factors. Many intrinsic antibodies are considered to be the targets of these antibodies, especially type 2 collagen, actinium, and whooping cough. The most famous one of these antibodies is CTL2-like protein, a diabetic protein of the inner ear.[37,38]

Autoimmune diseases may cause various kinds of conflicts in and outside the target organ, and some evidence suggests that autoimmune diseases, like systemic lupus erythematosus, rheumatoid arthritis, and vitiligo, may damage the sensorineural nerves and cause sensorineural deafness. However, this relationship is not clearly defined. Therefore, we performed this meta-analysis to investigate the association between SNHL and these autoimmune diseases. The outcomes of our study revealed that the prevalence of SNHL in SLE cases was 21.26 [3.80, 38.71]%, which was statistically significant, and pooled analysis of ORs observed in individual studies showed that the odds of SNHL prevalence was 12.11 [7.4, 24.12] ($P < .001$). The prevalence of SNHL in RA cases was 16.14 [−9.03, 41.31]%, which was statistically significant, and pooled analysis of ORs observed in individual studies showed that the odds of SNLH prevalence was 2.23 [1.84, 2.32] ($P < .001$). Furthermore, the prevalence of SNHL among vitiligo cases was 38.80 [22.36, 55.25]%, which was statistically significant, and pooled analysis of ORs observed in individual studies showed that the odds of SNHL prevalence was 5.82 [3.74, 9.68] ($P < .001$). The findings derived from the present study demonstrated that SNHL was significantly related to the autoimmune diseases of systemic lupus erythematosus, rheumatoid arthritis, and vitiligo, and routine SNHL evaluation should be required for these cases.

The treatment for SNHL related to autoimmune diseases is similar to that for SSNHL, which is systemic corticosteroids. If systemic corticosteroids fail or are contraindicated for some cases, transtympanic infusion and non-steroid immunosuppressant drugs may be considered.[39] However, many cases are irresponsive to steroids. Even if the cases are responsive, clinical response to steroid treatment mainly exists during the early period .[40] If the results are still unsuccessful after all the above treatments and cases develop profound bilateral SNHL, cochlear implantation may be considered.[41]

It should be noted that there are several limitations to this study. First, only the relationship between SNHL and systemic lupus erythematosus, rheumatoid arthritis, and vitiligo was documented in this meta-analysis. The relationship between SNHL and other rare autoimmune diseases remains to be investigated due to limited evidence. Second, the novel treatment of SNHL related to autoimmune diseases was not investigated in this study. Third, the exact pathogenic mechanism of autoimmune diseases causing SNHL remains to be investigated.

CONCLUSION

The results of the present study revealed that SNHL is significantly correlated with the autoimmune diseases of systemic lupus erythematosus, rheumatoid arthritis, and vitiligo. These cases need a routine evaluation of SNHL.

Data Availability: The data behind the findings of this present study are available on demand from the corresponding author.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – X.L., D.Y.; Design – X.L., Z.C.; Supervision – F.Z.; Funding – Z.C.; Materials – X.L., F.C.; Data Collection and/or Processing – X.L., Z.C.; Analysis and/or Interpretation – F.C., D.Y.; Literature Review – X.L., Z.C.; Writing – X.L.; Critical Review – F.Z.

Acknowledgments: Dr Zuiwei Cao was awarded National Natural Science Foundation of China (81860871).

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This work was supported by National Natural Science Foundation of China [81860871].

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