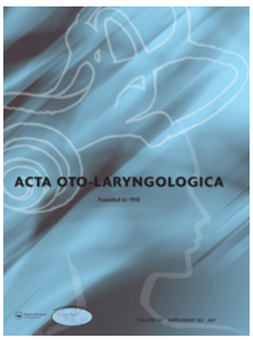

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RESEARCH ARTICLE

Idiopathic sudden sensorineural hearing loss and acute low-tone sensorineural hearing loss: a comparison of the results of a nationwide epidemiological survey in Japan

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ABSTRACT

Objectives: The aim of this study was to investigate the differences between idiopathic sudden sensorineural hearing loss (SSNHL), and acute low-tone sensorineural hearing loss (ALHL) using the results of a nationwide survey database in Japan and to analyze the variables associated with their clinical features and the severity of hearing impairment, treatment, and prognosis.

Methods: Participants were patients registered between April 2014 and March 2016 in a multicenter epidemiological survey database involving 30 university hospitals and medical centers across Japan. Statistical analysis was performed to clarify the factors associated with their clinical characteristics and the severity of hearing impairment, treatment, and prognosis.

Results: Idiopathic SSNHL and ALHL differed significantly in terms of male-to-female ratio, age distribution, and time from onset to start of treatment. The treatment methods and hearing prognosis also differed markedly between the two diseases. A majority (92%) of idiopathic SSNHL patients were administered some type of corticosteroid, while half of the ALHL patients received corticosteroids and a diuretic agent.

Conclusion: The results suggested that idiopathic SSNHL and ALHL belonged to different categories of inner ear disease.

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KEYWORDS
Idiopathic sudden sensorineural hearing loss; acute low-tone sensorineural hearing loss; epidemiological survey; severity of hearing impairment; treatment

Introduction

Sudden-onset sensorineural hearing loss consists of two similar clinical entities; idiopathic sudden sensorineural hearing loss (SSNHL) and acute low-tone sensorineural hearing loss (ALHL). Idiopathic SSNHL is defined as hearing levels for SSNHL of 30 dB or more over three consecutive frequencies [1,2].

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Table 1. Criteria for diagnosis of sudden deafness.

Main symptoms
Sudden onset
Sensorineural hearing loss, usually severe
Unknown etiology
For reference
Hearing loss (i.e., hearing loss of 30 dB or more over three consecutive frequencies)
Sudden onset of hearing loss, but may progressively deteriorate over 72 h
No history of recurrent episodes
Unilateral hearing loss, but may be bilateral at the onset
May be accompanied by tinnitus
May be accompanied by vertigo, nausea, and/or vomiting, without recurrent episodes
No cranial nerve symptoms other than from cranial nerve VIII
Definite diagnosis: all of the above main symptoms are present

These criteria were established by the Research Committee of the Ministry of Health, Labour and Welfare of Japan in 2012.

Table 2. Criteria for diagnosis of acute low-tone sensorineural hearing loss without vertigo.

Main symptoms
1. Acute or sudden onset of cochlear symptoms including ear fullness, tinnitus, and hearing loss
2. Low-tone hearing loss
3. Without vertigo
4. Unknown cause
For reference
1. Audiometric criteria of low-tone hearing loss.
(1) The sum of hearing levels at low frequencies of 0.125, 0.25, and 0.5 kHz is 70 dB or more.
(2) The sum of hearing levels at high frequencies of 2, 4, and 8 kHz is 60 dB or less.
2. Cochlear symptoms may be recurrent.
3. May progress to Ménière's disease.
4. May be accompanied with light dizzy sensation.
5. May be bilateral.

Definite: All of the main symptoms. Audiometric criteria (1) and (2).
Probable: All of the main symptoms. Audiometric criteria (1) and the same hearing levels at high frequencies of 2, 4, and 8 kHz as the contralateral ear.
These criteria were established by the Research Committee of the Ministry of Health, Labour and Welfare of Japan in 2011.

However, a proportion of the patients whose initial audiograms met these criteria also met the criteria for ALHL (see Table 1 in [3]). ALHL is characterized by acute onset low-tone hearing loss often associated with tinnitus, ear fullness, and/or autophony. A series of reports have suggested that ALHL is correlated with endolymphatic hydrops or Ménière's disease (MD) and the clinical characteristics and hearing prognosis of ALHL differ from those of idiopathic SSNHL [4–6]. In this study, to investigate the differences between these two inner ear diseases, we compared SSNHL and ALHL from both a clinical and epidemiological perspective using a multi-center large cohort database involving 21 university hospitals and four medical centers.

Materials and methods

The subjects for this analysis were patients (3419 idiopathic SSNHL and 931 ALHL) registered in the multicenter database between April 2014 and March 2016. Twenty-one university hospitals and four medical centers participated in this epidemiologic survey. The recorded data included sex, age, body height, weight, affected side, date of onset, onset age, pure-tone audiogram, past history, and treatment. Hearing thresholds were measured at octave intervals between 125 Hz and 8 kHz. Initial and final audiograms were requested for all patients. All data, including the hearing thresholds in the audiograms, were entered into a computer database. From the audiogram data, the grade of the initial audiogram and the recovery rate, as defined by the Ministry of Health and Welfare in Japan [7], were obtained. In some cases, the clinical data were incomplete, but our analysis included the available data for each category in such cases.

Idiopathic SSNHL and ALHL were defined according to the criteria established by the Sudden Deafness Research Committee of the Ministry of Health and Welfare, Japan (2012, 2011) as listed in Tables 1 and 2. Criteria for the severity of hearing loss in ALHL used in this study are shown in Table 3.

The study protocol was approved by the Ethics Review Committee of Nagoya University as well as those of all the other universities. The data were analyzed using SPSS 24.0 for Windows (SPSS, Chicago, IL, USA). Statistical analysis was performed using the available data in each category, using a χ^2 test and Student's t-test. The level of significance was set at $p < .05$.

Table 3. Criteria for the severity of hearing loss in acute low-tone sensorineural hearing loss (ALHL) (the Research Committee of the Ministry of Health and Welfare for Acute Profound Deafness, 2005).

Grade	Criteria
1	The sum of hearing levels at 3 low-tone frequencies <100 dB
2	100 dB ≦ The sum of hearing levels at 3 low-tone frequencies <130 dB
3	130 dB < The sum of hearing levels at 3 low-tone frequencies <160 dB
4	The sum of hearing levels at 3 low-tone frequencies ≧160 dB

Results

Prior to detailed analysis, we performed data cleaning of both the idiopathic SSNHL and ALHL registered data. As a result of data cleaning, 67 cases registered as idiopathic SSNHL were found to fulfill the defined ALHL criteria and 36 cases registered as idiopathic SSNHL fulfilled the probable ALHL criteria. To aid in making a more precise comparison, we removed these 103 cases from the idiopathic SSNHL group in the further analysis.

A comparison of the clinical characteristics in 3316 idiopathic SSNHL (male: 1719, female: 1556) and 931 ALHL (male: 241, female: 523) patients is presented in Table 4. The age of disease onset in patients with ALHL was significantly younger than that for idiopathic SSNHL. The mean onset age of idiopathic SSNHL was 54.5 years (SD =17.0) whereas the mean onset age of ALHL was 38.0 years (SD =18.8).

The proportion of women with ALHL was significantly higher than that with idiopathic SSNHL. For all participants, the female:male ratio was 0.91:1 for SSNHL and 2.17:1 for ALHL. In patients <60 years old, the female:male ratio was 0.89:1 for SSNHL and 2.36:1 for ALHL (Figure 1(A) and (B)). These data indicated that there is a female predominance in ALHL ($p < .01$). The number of bilateral affected cases was significantly higher among the ALHL cases ($p < .05$) and the

time from onset to start of treatment was significantly longer for ALHL (mean: 13.5 days) than for idiopathic SSNHL (mean: 6.5 days) ($p < .01$).

The initial and final average hearing thresholds at each frequency for SSNHL and ALHL are shown in Figure 2(A) and (B). Both the initial and final average PTA for all frequencies were worse for idiopathic SSNHL than for ALHL. In idiopathic SSNHL, the final average hearing thresholds for high tones were relatively poorer than those for low tones.

Table 4. Characteristics of the included patients.

	Sudden sensorineural hearing loss		Acute low-tone hearing loss	
	Number	Percentage (%)	Number	Percentage (%)
All patients	3316		931	
Sex*				
Male	1719	52.5	241	31.5
Female	1556	47.5	523	68.5
Affected ear				
Right*	1504	46.5	352	38.0
Light	1702	52.6	521	56.2
Bilateral*	30	0.9	54	5.8
Age				
≦15*	80	2.6	159	17.5
16–64*	2049	65.5	663	72.9
≧65*	999	31.9	87	9.6
Time from onset to the start of treatment				
≦7 days*	2585	82.0	454	70.2
8–14 days	397	12.5	77	11.9
≧15 days*	184	5.6	116	17.9
Symptom				
Tinnitus*	2378	77.8	414	64.6

*$p < .05$.

Systemic corticosteroids are commonly used to treat patients with acute sensorineural hearing loss (Kitoh et al. [8], in this special issue). In idiopathic SSNHL patients, systemic steroids were the primary treatment, with intratympanic steroids chosen for salvage and substitute treatment (Kitoh et al. [8], in this special issue). However, in ALHL patients, systemic or intratympanic steroids were used in only 54.1% and diuretic agents were used in 63.8% of patients. Combined treatment with steroids and diuretic agents was given in 31.4% of patients and diuretic therapy alone in 27.9% of patients (Figure 3). The rates of complete recovery for ALHL patients were 72.0% in the systemic steroid group and 83.1% in the diuretic-only group. However, 41.3% of patients in the systemic steroid group had Grade 3 or 4 ALHL, while only 22.8% of patients in the diuretic-only group had Grade 3 or 4 ALHL. Most patients were simultaneously treated with vitamin B12 and adenosine triphosphate. The detailed treatments outcome of SSNHL and ALHL are described in other papers in this supplement [8–10].

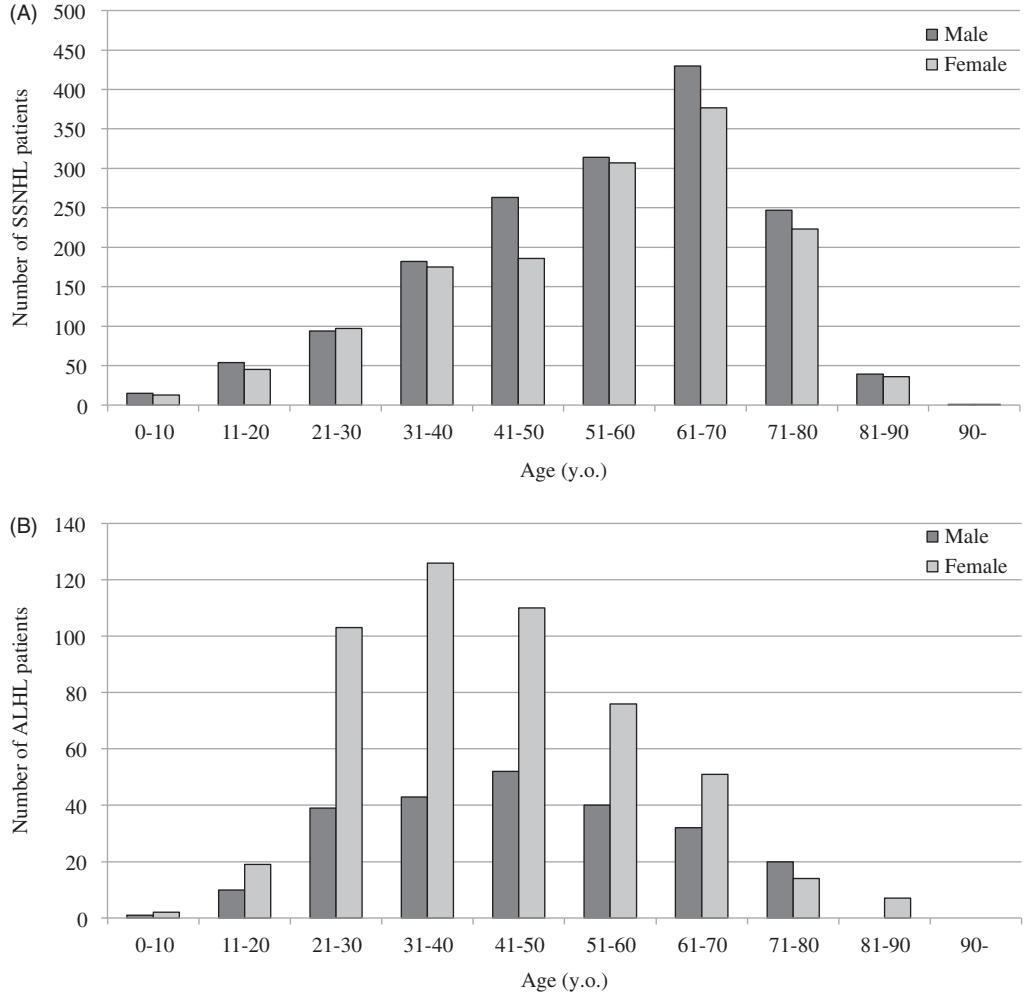

Figure 1. (A) Distribution of the incidence of SSNHL in males and females in each group. (B) Distribution of the incidence of ALHL in males and females in each group.

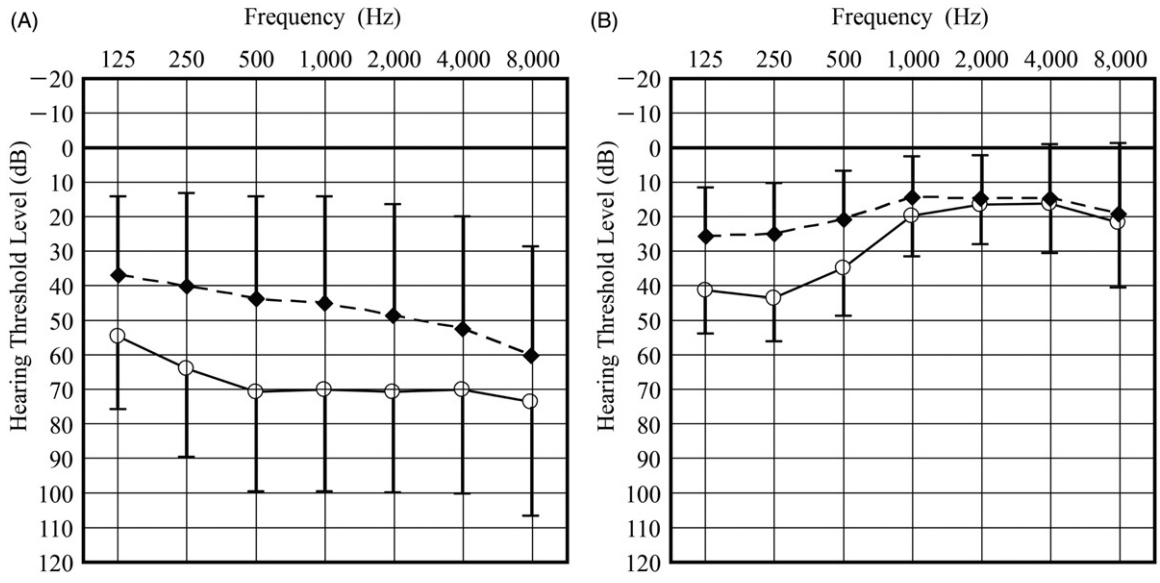

Figure 2. (A) Average of initial and final pure tone audiograms for SSNHL patients. Initial average pure tone audiogram: solid line; final average pure tone audiogram: dotted line. (B) Average of initial and final pure tone audiograms for ALHL patients. Initial average pure tone audiogram: solid line; final average pure tone audiogram: dotted line.

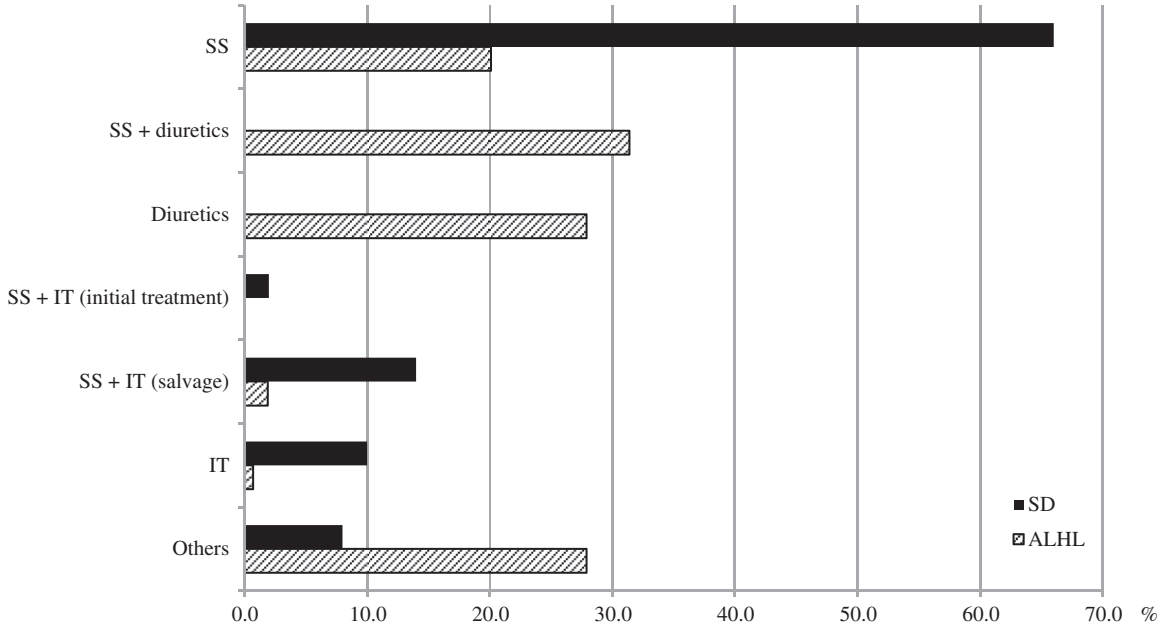

Figure 3. Comparison of the treatment modalities for SSNHL and ALHL. SS: systemic steroids; IT: intratympanic steroids; diuretics: diuretic agent.

Discussion

The present results showed a clear difference between idiopathic SSNHL and ALHL in both clinical and epidemiological terms. Possible etiologies of SSHNL include viral infection, vascular impairment, autoimmune disease, inner ear pathology, and central nervous system anomalies, although the cause in most patients is never identified [11]. On the other hand, ALHL has been hypothesized to be associated with endolymphatic hydrops on the basis of electrophysiological and audiological characteristics [4–6]. Yamasoba et al. [4] reported that ALHL patients frequently present with abnormal results for functional tests, such as the glycerol test or electrocochleography, and that over the long term, some patients develop cochlear or classic MD. Some reports have suggested similar clinical features or abnormal functional test results in ALHL patients and that ALHL may be caused by endolymphatic hydrops confined to the cochlea [6]. Recent studies using magnetic resonance imaging have demonstrated that some patients with ALHL have evidence of endolymphatic hydrops [3].

The incidence of idiopathic SSNHL was highest in older men, and that of ALHL was highest in younger women. These observations supported the view that some idiopathic SSNHL may be related to vascular disease, particularly as the rate of cardiovascular events increases with age [12].

Our study showed a significant female predominance in ALHL patients, which is in agreement with the results of a previous study [7]. The question of gender difference has

been discussed for MD patients [13], and a hormonal influence on MD has been suggested. In epidemiological studies, the gender difference in ALHL appears similar to that for MD. Nakashima et al. [2] reported that among patients under 60 years of age, idiopathic SSNHL was more frequent in women than in men. This tendency was associated with the incidence of confirmed ALHL in young women. This must be viewed with some caution, however, as their study included only idiopathic SSNHL patients who visited private clinics. Therefore, there may be a certain sampling bias; i.e., this population might comprise mild cases and/or those associated with endolymphatic hydrops or MD.

We analyzed hearing recovery after treatment for idiopathic SSNHL [7]. The average hearing level of idiopathic SSNHL patients was Grade 3 to Grade 2, according to these criteria, and it was found to improve by about 23 dB (slight improvement). In our study, idiopathic SSNHL had a poor hearing prognosis compared to that for ALHL, as shown in Figure 2(A) and (B).

Diverse treatments have been considered for SSNHL and ALHL. Corticosteroids are a commonly used treatment for SSNHL in Japan [2,14]. Recently, intratympanic steroid administration has been used for some cases [15–17]. In our study, most idiopathic SSNHL patients received systemic steroids as a primary treatment, whereas a combination of systemic steroids and diuretic agents was mainly used for ALHL patients. For cases of severe ALHL, systemic steroids alone or a combination of steroids and diuretic agents were frequently administered. Despite the fact that corticosteroids have been used as the general treatment modality for idiopathic SSNHL in Japan [2,14], the evidence for steroid treatment is controversial with no significant difference in hearing prognosis found in comparison with other treatments [18–20]. To improve the treatment of SSNHL, it is important to clarify its pathophysiology. With regard to ALHL treatment, diuretic agents have been used in addition to corticosteroids [21] as endolymphatic hydrops is speculated to be an etiology for ALHL as it is for MD [3,5].

Our large clinical database revealed differences in the characteristics of patients with idiopathic SSNHL and ALHL; however, idiopathic SSNHL and ALHL may include various pathophysiological states. Future physiological and imaging studies are needed to clarify the pathophysiological conditions responsible for these inner ear diseases.

Conclusions

The etiologies of idiopathic SSNHL and ALHL remain unclear. However, the present epidemiological survey suggested that there are clear differences between these two inner ear diseases, and that some ALHL patients should be treated as early stage MD.

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Disclosure Statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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