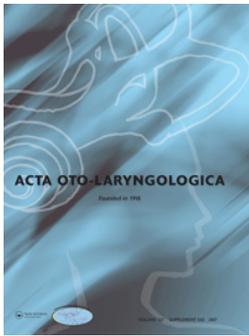


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ABSTRACT

Objectives: A nationwide epidemiological survey involving 23 hospitals in Japan was conducted and the predictive values of demographic data were examined statistically.

Methods: A total of 642 patients from 23 hospitals, including 20 university hospitals, in Japan were enrolled in the study. Age ranged from 8 to 87 years, and all were diagnosed with acute low-tone sensorineural hearing loss (ALHL) between 1994 and 2016. Demographic data for the patients, such as symptoms, gender, mean age, and distribution of ALHL grading, were collected and analyzed in relation to prognosis using Student's *t*-test, χ^2 test and logistic regression.

Results: Female gender ($p < .013$), younger age ($p < .001$), low-grade hearing loss ($p < .001$), and shorter interval between onset and initial visit ($p < .004$) were significantly predictive of a good prognosis. The prognosis for definite ALHL was significantly better than that for probable ALHL ($p < .007$).

Conclusions: The severity of initial hearing loss, interval between onset and initial visit and age were important prognostic indicators for ALHL, while female gender was an important prognostic indicator peculiar to ALHL.

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Introduction

In 1982, Abe reported that all 39 consecutive patients with acute low-tone sensorineural hearing loss (ALHL) of unknown origin showed complete recovery (CR) without fluctuation or recurrence [1]. He proposed ALHL as a distinct clinical entity from idiopathic sudden sensorineural hearing loss (SSNHL) in that the hearing loss is limited to low-tone frequencies and shows a good prognosis. Yamasoba et al., on the other hand, reported that recurrence or fluctuation was common and developed to typical

Meniere's disease in some of ALHL patients over a long-time follow-up period, suggesting that ALHL may be caused by cochlear endolymphatic hydrops [2].

The incidence of definite ALHL is reported to be 42.8–65.8 per 100,000 population in Japan [3] and to account for 18% of idiopathic SSNHL patients in Japan [4]. ALHL is a common presentation, but it has not received much attention in the literature with no large-scale epidemiological studies of ALHL, in particular, reported to date. This is speculated to be due to the fact that the

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prognosis for ALHL is far better than that for idiopathic SSNHL, and ALHL is not recognized as an independent clinical entity in most countries apart from Japan. Herein, we present the epidemiological characteristics of as well as the prognostic indicators for ALHL.

Patients and methods

In the multi-center database between April 2014 and March 2016, 931 ALHL patients were registered. The inclusion criteria used in this study, the severity of ALHL, and hearing improvement criteria in ALHL are shown in Tables 1–3. These criteria were based on the criteria proposed by the Research Committee of the Ministry of Health, Labour and Welfare in Japan. We excluded patients whose data were incomplete for analysis. Per these criteria, 642 patients with ALHL from 23 participating hospitals, including 20 university hospitals, in Japan were registered and enrolled in this study. They ranged in age from 8 to 87 years with the mean of 43.8 years. The study protocol was approved by the Ethics Review Committees of 3 hospitals and 20 universities.

Demographic data were summarized for categorical and continuous measures. Means and ranges are presented for continuous data. Categorical variables are presented as numbers. The prognosis for ALHL (binary outcome) was examined

in relation to the demographic characteristics using logistic regression. Student's *t*-tests were used to compare continuous variables, and categorical data were compared among more than two groups using a χ^2 test. Analysis was undertaken for the complete recovery (CR) group and the remaining three non-CR (improvement + no change + deterioration) groups.

Logistic regression was used to examine the association between the prognosis for ALHL (as a dependent variable) and the grading of hearing loss and physical disease outcomes including whether the patients had diabetes mellitus or hypertension. The relationship between prognosis for ALHL and whether the patients worked nightshift was also analyzed using logistic regression analysis. Values of <0.05 were considered significant. All analyses were conducted using SPSS software (IBM SPSS Statistics 24 for Windows, Advanced Analytics Inc., Tokyo, Japan).

Results

The demographic data for 642 ALHL patients are presented in Table 4. Patients consisted of 205 males and 433 females (gender was not identified in 4 patients), indicating a marked gender preponderance with a male-to-female ratio of 1–2.1. The patients ranged in age from 8 to 87 years,

Table 1. Inclusion criteria for the ALHL (the Research Committee of the Ministry of Health and Welfare for Acute Profound Deafness, 2011).

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.	

Table 2. Criteria for the severity of hearing loss in 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	$100 \text{ dB} \leq$ The sum of hearing levels at 3 low-tone frequencies <130 dB
3	$130 \text{ dB} <$ 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

Table 3. Hearing improvement criteria for ALHL (the Research Committee of the Ministry of Health and Welfare for Acute Profound Deafness, 2012).

Evaluation	Criteria
Complete recovery	All 3 low-tone frequencies of final audiograms are 20 dB or less, or improvement to the same degree of hearing in the unaffected ear
Improvement	Mean hearing level of 3 low-tone frequencies improves more than or equal to 10 dB, but not completely recovered
No change	Mean hearing level of 3 low-tone frequencies improves less than 10 dB
Deterioration	Other than the above criteria

Table 4. Demographic characteristics of ALHL patients.

Gender	Male	205	
	Female	433	
	Unknown	4	
Mean age	Total	43.8 \pm 15.5	
	Male	46.1	
	Female	42.6	
Side	Right	251	
	Left	345	
	Bilateral (simultaneity)	39	
	Bilateral (heterochrony)	4	
	Unknown	3	
Criteria (<i>n</i> = 635)	Definite	564	
	Probable	71	
	Severity (<i>n</i> = 640)	Grade 1	210
		Grade 2	211
Grade 3		128	
Outcome (<i>n</i> = 640)	Grade 4	91	
	Complete recovery	432	
	Improvement	83	
	No change	84	
Symptoms	Deterioration	41	
	Tinnitus (<i>n</i> = 640)	Yes	387
		No	209
		Unknown	46
	Ear fullness (<i>n</i> = 639)	Yes	484
No		105	
Unknown		52	
Dizziness (<i>n</i> = 640)	Yes	73	
	No	536	
	Unknown	31	
Hyperacusis (<i>n</i> = 640)	Yes	102	
	No	346	
	Unknown	192	

Table 5. Multinomial logistic regression analysis of ALHL outcomes based on demographic characteristics.

Characteristic	<i>p</i>	OR	95% CI
Younger age	<.001	0.97	0.96–0.98
Female gender	.013	0.59	0.36–0.78
Shorter interval from onset	.004	0.99	0.99–0.10
Severity (Low-grade of severity)	<.001	0.58	0.49–0.70
Criteria for ALHL (Definite ALHL)	.007	0.47	0.27–0.82
Dizziness	.557	1.15	
Diabetes mellitus	.274	1.63	
Hypertension	.367	2.40	
Nightshift	.061	2.03	
Hyperacusis	.006	0.84	0.74–0.95

with a mean age of 43.8 ± 15.5 years. The mean age of males was 46.1, which was older than that of the female patients (42.6 years), although the difference was not significant. Hearing loss occurred in the right ear in 251 patients, in the left ear in 345 patients and bilaterally in 43 patients (39 simultaneous and 4 heterochronous onsets). Out of 635 patients, 564 patients (88.9%) were diagnosed as definite ALHL, with the remaining 71 (11.1%) diagnosed as probable ALHL. The severity of hearing loss was Grade 1 in 210 (32.8%), Grade 2 in 211 (33.0%), Grade 3 in 128 (20.0%), and Grade 4 in 91 (14.2%). Four hundred and thirty-two (67.5%) patients recovered completely (Complete recovery), 83 (13.0%) patients showed improvement but not a CR (Improvement), 84 (13.1%) patients showed no improvement (No change), and the remaining 41 (6.4%) patients showed deterioration (Deterioration). Regarding clinical symptoms, 387 (60.5%) patients experienced tinnitus, 484 (75.7%) ear fullness, 73 (11.4%) dizziness, and 102 (15.9%) hyperacusis. Among these four symptoms, ear fullness was the most frequent symptom. Multinomial logistic regression analysis of ALHL outcomes based on the demographic characteristics is presented in Table 5.

Younger age (OR: 0.97; CI: 0.96–0.98; $p < .001$), female gender (OR: 0.53; CI: 0.36–0.78; $p < .013$), shorter interval between onset and initial visit (OR: 0.99; CI: 0.99–1.0; $p < .004$), low-grade hearing loss (OR: 0.58; CI: 0.49–0.70; $p < .001$), definite ALHL (OR: 0.47; CI: 0.27–0.82; $p < .007$) and hyperacusis (OR: 0.84; CI: 0.74–0.95; $p < .006$) were significantly predictive of a good prognosis.

A comparison of demographic characteristics between the CR and three non-CR (improvement + no change + deterioration) groups is presented in Table 6. Patients in the CR group ($n = 432$) were significantly younger ($p < .001$), showed a shorter interval from onset to initial visit ($p = .01$) and a lower grade of hearing loss than did those in the non-complete recovery (non-CR) groups ($n = 208$). Definite ALHL ($p < .001$) and absence of hypertension ($p = .013$) were significantly more frequent in the CR group than in the non-CR groups. Other demographic characteristics, such as diabetes mellitus, working nightshift and alcohol consumption, were not related to hearing outcome.

Discussion

It is generally accepted that the severity of initial hearing loss, interval between onset and initial visit (i.e. an early start to treatment) and younger age are important indicators of a

Table 6. Comparison of demographic characteristics between the CR and non-CR groups.

	CR	Non-CR	<i>p</i>	No.
Mean age	40.43 ± 14.22	50.54 ± 15.84	<.001*	$n = 642$
Interval from onset (day)	10.71 ± 28.85	20.93 ± 46.56	.010*	$n = 602$
Severity (dB)	110.37 ± 32.57	135.14 ± 38.24	.009*	$n = 639$
Gender (M:F)	116:314	89:118	<.001#	$n = 637$
Grade 1:2:3:4	181:137:77:37	29:74:51:54	<.001#	$n = 640$
Criteria (D:P)	398:29	166:41	<.001#	$n = 634$
Hypertension (Y:N:U)	19:358:55	21:165:22	.013#	$n = 640$
DM (Y:N:U)	14:367:51	11:177:19	.082	$n = 639$
Nightshift (Y:N:U)	16:154:259	12:57:139	.070	$n = 637$
Alcohol (Y:N:U)	61:176:194	43:71:94	.690	$n = 639$
Tinnitus (Y:N:U)	266:138:28	119:71:18	.456	$n = 640$
Ear fullness (Y:N:U)	321:76:34	162:29:17	.498	$n = 639$

CR: complete recovery, D: definite, P: probable, Y: yes, N: no, U: unknown, DM: diabetes mellitus, $p < .05$ (*Student's *t*-test # χ^2 -test).

better prognosis for idiopathic SSNHL [5,6]. These prognostic indicators were found to hold true for ALHL in the present study. In addition, female gender and definite ALHL were also important prognostic indicators for ALHL. Definite ALHL does not involve high-tone hearing loss in accordance with the diagnostic criteria and, subsequently, most of definite ALHL patients are younger than those with probable ALHL. For this reason, definite ALHL might exhibit a better prognosis. A female gender preponderance has been reported as one of the epidemiologic characteristics of ALHL [2,3,7]. Such sexual preponderance was demonstrated in the present study. The mean age of female ALHL patients was 2.3 years younger than that of the male patients, but this difference in mean age between females and males was not significant. Therefore, female gender seems to be an independent variable that predicts a good prognosis.

Other demographic characteristics, such as clinical symptoms, presence of hypertension or diabetes mellitus, alcohol consumption and working nightshift, were found to be unrelated to prognosis for ALHL. Multinomial logistic regression revealed that hyperacusis was related to a worse hearing outcome; however, this association was not observed in the analysis using the χ^2 test. Conversely, hypertension was found to be a worse indicator by χ^2 test, but this was not confirmed by multinomial logistic regression analysis. Therefore, it is questionable whether these two indicators are good prognostic indicators for ALHL.

In conclusion, the severity of initial hearing loss, interval between onset and initial visit and age were important prognostic indicators for ALHL, as with idiopathic SSNHL, while female gender was an important prognostic indicator peculiar to ALHL.

Disclosure statement

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

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