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Research Paper

Analysis of thyroid dysfunction in patients with sudden sensorineural hearing loss

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KEYWORDS
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Abstract *Background:* Sudden sensorineural hearing loss (SSHL) refers to the sudden occurrence of unexplained sensorineural hearing loss. The present study showed that different systemic diseases had different influence on the occurrence and hearing outcome of SSHL. Thyroid hormone is one of the important factors for the development of fetal ear and auditory function. However, the distribution of thyroid dysfunction in SSHL patients and the effect of thyroid dysfunction on the occurrence and hearing outcome of SSHL has not been studied.
Methods: In this study, a retrospective analysis had been done in 676 patients with SSHL. We had described the distribution of thyroid function in patients with SSHL in detail, and by the statistical method, analyzed the relationship between the hearing outcome and thyroid dysfunction, respectively.
Results: In all patients, 24.41% (165/676) had abnormal thyroid function testing results. The onset age of SSHL in FT3 abnormal group (including low and high group) was younger than that in normal FT3 group. Recovery group had more patients with lower-than-normal T3 level as compared to non-recovery patients. Significant associations between T3 levels and hearing outcome were observed in the subgroup with longer time elapse between symptom onset

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and treatment (≥14 d).
Conclusion: The incidence of thyroid dysfunction in SSHL is significantly higher than in the general population. There was obvious relationship between T3 and FT3 item of thyroid dysfunction and the onset time and hearing outcome of SSHL, which indicated that T3 or FT3 indicator may be one of the affecting factors for the SSHL. Early screening and diagnosis of thyroid dysfunction, especial T3 level, may help to evaluate the prognosis in SSHL patients.

Introduction

Sudden sensorineural hearing loss (SSHL) refers to the sudden occurrence of unexplained sensorineural hearing loss in 72 h, at least in adjacent two frequencies have hearing loss greater than 20 dB HL.[1] In recent years, with the changes in the pace and manner of life, the incidence of SSHL in the world has gradually increased. The incidence of SSHL in the United States is 5/100 000—20/100 000, and there are about 4000 to 25 000 new cases every year. The incidence in Japan has increased from 3.9/100 000 to 27.5/100 000 in 1972. The incidence in China is also increasing year by year, but lack large sample epidemiological investigation. The cause of SSHL and pathological physiological mechanism has not been fully elucidated, many factors may cause SSHL. At present, the accepted etiologies and the possible mechanisms include: the inner ear vasospasm, vascular dysfunction, vascular embolization or thrombosis, membranous labyrinth and hair cell injury.[2] Meanwhile, different systemic diseases had different influence on the occurrence and hearing outcome of SSHL. In all system of human body, the thyroid is an important part of endocrine system, thyroid hormone is one of the important factors for the development of fetal ear and auditory function. There were 25% patients showed the different types of hearing impairment with congenital thyroid function. The risk of hearing loss was closely related to the severity of the thyroid dysfunction.[3] However, what distribution of thyroid dysfunction is in patients with SSHL? Is the severity, hearing loss typing and hearing outcome of SSHL patients with thyroid dysfunction the same as those with normal thyroid function? There were very few studies. In this study, the above problems were analyzed.

Methods

Subjects

We performed a retrospective study of consecutive inpatient cases with SSHL who were treated between January 2008 and December 2015 in our hospital. The inclusion criteria consisted of several parameters according to the Editorial Board of Chinese Journal of Otorhinolaryngology Head and Neck Surgery: (1) SSHL >20 dB affecting >2 consecutive frequencies of pure-tone thresholds within 72 h; (2) no definite cause (including systemic or local factors) was found; (3) it can be accompanied by tinnitus, fullness, dizziness, nausea, vomiting, and abnormal sensation of the ear skin; (4) excluding acoustic neuroma, craniocerebral trauma, window rupture, drug intoxication, etc. A total of 676 cases were investigated in this study. All participants provided informed consent in accordance with the Ethics Committee of Chinese PLA General Hospital.

Auditory evaluation

The hearing level was calculated by the average air-conduction hearing thresholds across 500 Hz to 4000 Hz frequencies and graded,[1] including: mild: 20—40 dB HL; moderate: 41—70 dB HL; severe: 71—95 dB HL; profound: > 95 dB HL. In no response cases, calculations were made by adding 5 dB to the maximum level of sound generated by the audiometer. The patterns of hearing loss have been categorized into five audiogram configurations: (1) ascending (the average threshold between 250 and 500 Hz was 20 dB higher than the mean threshold of 4000—8000 Hz); (2) descending (the average threshold between 4000 and 8000 Hz was 20 dB higher than the mean threshold of 250—500 Hz); (3) flat (similar thresholds observed across the entire frequency range and the average hearing threshold not exceeding 80 dB HL); (4) profound (similar thresholds observed across the entire frequency range and the average hearing threshold over 80 dB HL); and (5) irregular type (any audiograms unqualified to be categorized into the above four types).

Thyroid function tests

Hematological examination included routine blood test, biochemical examination, immune antibody and cytomegalovirus antibody, EB virus antibody, thyroid function test. Complete blood was tested for all participants on the first morning after admission. We obtained thyroid function data for seven items of thyroid function or five items by Siemens ADVIA Centaur XP automatic immunoassay system. The normal reference range is as follows: serum thyroxine (T4) is 55.34—160.88 nmol/L, serum triiodothyronine (T3) 1.01—2.95 nmol/L, serum free T3 (FT3) 2.76—6.30 pmol/L, serum free T4 (FT4) 10.42—24.32 pmol/L, thyroid stimulating hormone (TSH) 0.35—5.50 mU/L, antithyroglobulin antibodies (TGAb) < 60 IU/ml, antithyroid peroxidase antibodies (TPOA) < 60 IU/ml. According to the changes of thyroid function, all patients were divided into thyroid function normal group and thyroid function abnormal

group, and then divided into normal, low and high group according to each item.

Treatments and hearing outcome judgment

All hospitalized patients were treated with similar protocols as previously described.[4] Administered medications did not differ across groups. Based on the results of pure tone audiometry after treatment, all the studied objects were divided into two groups, the recovery group: the average hearing improve level $\geq$15 dB HL (total = heal + significant effective + effective), and the non-recovery group: the average hearing improve level $<$ 15 dB HL.

Statistical analysis

Data distributions were evaluated for normality by P-P (probability) plots and Q-Q (quantile) plots. *Levene's* test was used to assess the homogeneity of variance for a variable calculated for groups. For continuous variables with normal distribution, we evaluated the differences in patient characteristics using analysis of variance in cases of homoscedasticity and *Welch's t*-test when *Levene's* test showed statistical significance ($P < 0.05$), while *Kruskal—Wallis* test was used in non-normally distributed variables. On the other hand, the *Chi-square* test was conducted for categorical variables. All *P* values were two tailed, and differences were determined to be significant when $P < 0.05$. Unless otherwise stated, continuous variables with normal distribution were presented as means $\pm$ standard deviation (*SD*) or standard error (*SE*), while skewed distributed variables were expressed as median (interquartile range). All statistical analyses were estimated using the statistical software package SPSS 22.0 (IBM Corp, Armonk, NY, USA).

Results

General situation, classification and hearing outcome of SSHL

In this study, there were 676 cases of SSHL in total, male 334 cases (52.03%), and females 342 cases (47.93%). The age was between 6 and 85 years old, and the average was (45.4 $\pm$ 15.8) years. The time duration of the treatment was 1—195 days, with an average of (23.1 $\pm$ 25.5) days. All patients were described and counted the incidence and hearing outcome of SSHL in the hospital this time. There were 332 cases of left ear (49.11%) and 344 cases (50.89%) in the right ear. According to the audiogram types of hearing loss, there were the flat type 149 cases (22.04%), the descending type 141 cases (20.86%), the profound type 290 cases (42.90%), the irregular type 37 cases (5.47%), and the ascending type 59 cases (8.73%).

According to the results of pure tone audiometry before and after treatment respectively, we calculated every frequency in patients with pure tone hearing threshold (PTA), including the average threshold of hearing level before treatment (PTA.BT, initial hearing) and after treatment (PTA.AT, final hearing), then divided all patients into recovery group (303 cases, 44.82%) and non-recovery group (373 cases, 55.18%).

The statistical results of difference analysis of the general variables and hearing outcome of SSHL showed that there were significant differences between treatment recovery group and non-recovery group in time duration after onset of SSHL, PTA.BT, PTA.AT and audiogram type. Time duration was (14.1 $\pm$ 14.0) days in the recoveryeffective group and was (30.4 $\pm$ 30.1) days in non-recovery group. The PTA.BT was (87.4 $\pm$ 28.2) dB HL in the recovery group, (66.1 $\pm$ 32.9) dB HL in the non-recovery group. The PTA.AT was (52.5 $\pm$ 27.9) dB HL in the recovery group, (62.3 $\pm$ 33.2) dB HL in the non-recovery group. In recovery group, the profound type patients were the most (180 cases, 59.4%), the irregular type was the least (10 cases, 3.3%). However, in non-recovery group, the proportion of flat, descending and profound type was similar. They were 95 cases (25.5%), 100 cases (26.8%) and 110 cases (29.5%), respectively. Patients with irregular hearing loss was the least (27 cases, 7.2%). The above results are shown in Table 1.

Thyroid function examination results

In all patients, there were 310 patients (45.86%) tested five items of thyroid function and 366 cases (54.14%) tested seven items of thyroid function. 165 cases (24.41%) had thyroid dysfunction (abnormal thyroid item was greater than or equal to 1), while other 511 patients (75.59%) had normal thyroid function. Specific values and proportions as follows: TSH normal 613 cases (90.68%), low 36 cases (5.33%) and high 27 cases (3.99%); T3 normal 613 cases (90.68%), low 61 cases (9.02%) and high 2 cases (0.30%); T4

Table 1 Correlation analysis of the general situation and hearing outcome of SSHL.

Variables[a]	Recovery	Non-recovery	*P value*
Number (cases, %)	303 (44.82)	373 (55.18)	
Age of onset (years)	44.3 $\pm$ 16.0	46.3 $\pm$ 15.5	0.11
BMI (kg/m^2)	24.0 $\pm$ 3.7	24.4 $\pm$ 3.5	0.23
Time duration (days)	14.1 $\pm$ 14.0	30.4 $\pm$ 30.1	$<$0.001
Initial hearing (dB HL)	87.4 $\pm$ 28.2	66.1 $\pm$ 32.9	$<$0.001
Final hearing (dB HL)	52.5 $\pm$ 27.9	62.3 $\pm$ 33.2	$<$0.001
Gender			0.13
Female (cases, %)	155 (51.2)	169 (45.3)	
Male (cases, %)	148 (48.8)	204 (54.7)	
Affected side			0.854
Left (cases, %)	150 (49.5)	182 (48.8)	
Right (cases, %)	153 (50.5)	191 (51.2)	
Audiogram type			$<$0.001
Flat (cases, %)	54 (17.8)	95 (25.5)	
Descending (cases, %)	41 (13.5)	100 (26.8)	
Profound (cases, %)	180 (59.4)	110 (29.5)	
Irregular (cases, %)	10 (3.3)	27 (7.2)	
Ascending (cases, %)	18 (5.9)	41 (11.0)	

Continuous variables were presented as *mean* $\pm$ *SD* for normal distribution, or medians (interquartile range) for non-normal distribution. Categorical variables were presented as *n* (%).

[a] All the factors were analyzed by number of persons.

normal 660 cases (98.95%), low 11 cases (1.63%) and high 5 cases (0.74%); FT3 normal 661 cases (97.78%), low 4 cases (0.59%) and high 11 cases (0.30%); FT4 normal 665 cases (98.37%), low 7 cases (1.04%) and high 4 cases (0.59%); TPOA normal 273 cases (88.06%) and high 37 cases (11.94%); TGAb normal 282 cases (90.97%) and high 28 cases (9.03%). The statistical analysis results showed that there was no significant difference ($P > 0.01$) between thyroid function normal group and thyroid function abnormal group among the variables of the age of onset, BMI, PTA-BT, PTA-AT, the hearing gain, time duration and audiogram types.

Then according to each item of thyroid function, we had analyzed respectively the general variables in patients with SSHL and hearing situation. The results showed that the time duration was significant differences between groups ($P < 0.01$) within the T3 item group. It was (11.0 ± 11.7) days in low T3 group, significantly shorter than normal T3 group and high T3 group. Meanwhile within the FT3 item group, the onset age of SSHL was significant differences between groups ($P < 0.01$). It was (22.5 ± 11.0) years in low FT3 group and (23.4 ± 17.3) years in high FT3 group, significantly younger than FT3 normal group [(45.9 ± 45.9) years]. In addition to the above two items, we did not find significant differences in the other items between age, BMI, PTA-BT, PTA-AT, the hearing gain, time duration and audiogram types. The above results are shown in Table 2.

Correlation analysis between thyroid dysfunction and the hearing outcome of SSHL

According to the thyroid function, statistical analysis of each item and the relationship between the hearing outcome of SSHL had been done and the results showed that the hearing outcome of SSHL has significant difference ($P < 0.01$) in T3 groups. In addition to the above item, there was no difference in another six groups. The above results are shown in Table 3.

Significant associations between T3 levels and hearing outcome were only observed in the subgroup with longer time elapse between symptom onset and treatment (≥14 d)

According to univariate analysis (Table 4), well hearing outcome group had more patients with lower-than-normal T3 level as compared to non-recovery patients. Likewise, the simple linear model showed that low T3 level was associated with reduced risk of no recovery in SSHL patients [odds ratio (*OR*) 0.5, 95% confidence interval (*CI*) 0.3−1.0, $P = 0.048$). However, when confounding from age, gender, BMI, pre-treatment hearing and time duration were taken into account, the association between serum T3 and hearing outcome was no longer statistically significant. In a following step, we conducted stratified analysis by time duration. After adjustment, low T3 level was significantly associated with lower odds of non-recovery (*OR* 0.3, 95% *CI* 0.1−0.8) in the subgroup with longer time duration (≥14 d) compared with the euthyroid cases. In contrast, no significant was found in association between hearing outcome and T3 level in the subgroup with time duration less than 14 d. The sample size in higher-than-normal T3 group was not enough, and the associations with hearing outcome was not performed in this group.

Discussion

SSHL is one of the common diseases in outpatients of ENT. With the acceleration of social rhythm and the increase of life pressure, the incidence of SSHL increases year by year and shows a trend of getting younger than before years. Although all people with different ages may have suffer from SSHL, but the peak onset age of SSHL has certain differences in different groups and the objects of study. The foreign literature reported SSHL onset peaks usually was between the ages of five to sixty years.[1,2] Our country multicenter study showed the median onset age was 41 years, no obvious difference was found between the male to female.[1,5] In this study, the smallest onset age was 6 years old, and biggest was 85 years, the average was (45.4 ± 15.8) years. There was no statistically significant difference between recovery treatment group and non-recovery group. Meanwhile proportion of men (52.03%) and women (47.93%) was no statistical difference too.

As far as we know, the common causes of SSHL include: vascular disease, viral infections, autoimmune diseases, infectious diseases, cancer, etc. With the in-depth research, some risk factors like cardiovascular disease, blood rheology and high blood viscosity changes have also been gradually found associated with SSHL.[6,7] Based on a lot of multicenter studies showed that different types of SSHL hearing audiogram indicated different pathogenesis and different hearing outcome. Ascending type had the best hearing outcome, flat type was second, and descending and profound deafness were not very good.[8] In recovery group of our study, profound deafness type was the most (59.4%), irregular deafness patients were minimum (only 3.3%). And in non-recovery group, the proportion of profound type, flat type and descending type were similar, which was 95 cases (25.5%), 100 cases (26.8%) and 110 cases (29.5%), respectively. The irregular type was the least (27 cases, 7.2%). The difference of hearing audiogram in recovery and non-recovery group was statistically significant. Our result confirmed that the hearing audiogram type is one of the important factors that affect the prognosis of patients with SSHL.

Besides hearing audiogram type, another important accepted factor which affecting the hearing outcome of SSHL was treatment time duration after onset of SSHL, namely the sooner treatment after the onset of SSHL, the better the prognosis.[1,9] The average time duration of recovery group in this study was (14.1 ± 14.0) days after onset and (30.4 ± 30.1) days in non-recovery group. There was significant statistical difference between two groups. The above results showed that the treatment effectiveness of SSHL has significant relationship with the time duration before the start of treatment.

Is average threshold before treatment and after treatment (PTA.BT and PTA.AT), namely the severity of SSHL related to treatment effectiveness of SSHL? According to used report, the severer hearing loss, the poorer prognosis.[10] However, in our study, the PTA.BT in recovery group was significantly heavier than non-recovery group,

Table 2 Analysis of thyroid function in patients with SSHL.

Variables	Abnormal TFT (abnormal item $\geq$ 1)			TSH			
	No	Yes	*P* value	Normal	Lower	Higher	*P* value
Number (cases, %)	511 (75.59)	165 (24.41)		613 (90.68)	36 (5.33)	27 (3.99)	
Age of onset (years)	46.3 ± 15.7	42.8 ± 15.6	0.013	45.5 ± 15.9	40.4 ± 13.4	49.7 ± 15.2	0.060
BMI (kg/m^2)	24.3 ± 3.6	24.0 ± 3.8	0.442	24.2 ± 3.6	23.9 ± 3.9	24.9 ± 3.4	0.494
Initial hearing (dB HL)	74.0 ± 32.8	80.8 ± 31.5	0.025	75.4 ± 32.8	76.1 ± 29.9	81.2 ± 31.6	0.751
Final hearing (dB HL)	57.2 ± 31.3	59.9 ± 31.5	0.286	57.7 ± 31.4	55.3 ± 31.8	66.1 ± 29.4	0.238
Hearing gain (dB HL)	16.8 ± 19.0	20.9 ± 20.7	0.012	17.7 ± 19.4	20.8 ± 21.2	15.1 ± 18.2	0.624
Time duration (days)	24.4 ± 26.7	18.9 ± 21.2	0.008	23.8 ± 26.1	12.3 ± 9.7	22.2 ± 25.1	0.024
Audiogram type			0.166				0.353
Flat (cases, %)	109 (21.3)	40 (24.2)		129 (21.0)	10 (27.8)	10 (37.0)	
Descending (cases, %)	113 (22.1)	28 (17.0)		132 (21.5)	5 (13.9)	4 (14.8)	
Profound (cases, %)	210 (41.1)	80 (48.5)		262 (42.7)	18 (50.0)	10 (37.0)	
Irregular (cases, %)	29 (5.7)	8 (4.8)		35 (5.7)	2 (5.6)	0 (0.0)	
Ascending (cases, %)	50 (9.8)	9 (5.5)		55 (9.0)	1 (2.8)	3 (11.1)	

Variables	T3				T4			
	Normal	Lower	Higher	*P* value	Normal	Lower	Higher	*P* value
Number (cases, %)	613 (90.68)	61 (9.02)	2 (0.30)		660 (98.95)	11 (1.63)	5 (0.74)	
Age of onset (years)	45.8 ± 15.8	42.1 ± 14.9	23.5 ± 20.5	0.031	45.6 ± 15.8	37.5 ± 12.3	44.2 ± 5.1	0.244
BMI (kg/m^2)	24.2 ± 3.6	24.0 ± 3.6	22.2 ± 8.7	0.675	24.2 ± 3.6	24.1 ± 3.4	24.0 ± 2.8	0.985
Initial hearing (dB HL)	74.6 ± 32.3	86.0 ± 33.8	84.4 ± 52.1	0.025	75.5 ± 32.5	86.4 ± 29.9	69.2 ± 55.4	0.545
Final hearing (dB HL)	57.7 ± 31.1	58.9 ± 33.1	80.6 ± 50.4	0.668	57.8 ± 31.3	62.8 ± 26.5	61.2 ± 51.5	0.813
Hearing gain (dB HL)	16.9 ± 18.8	27.1 ± 23.2	3.8 ± 1.8	0.002	17.8 ± 19.5	23.5 ± 17.4	8.0 ± 11.1	0.166
Time duration (days)	24.2 ± 26.3	11.0 ± 11.7	40.0 ± 0.0	<0.001	23.2 ± 25.7	16.2 ± 15.8	28.8 ± 12.9	0.253
Audiogram type				0.251				0.593
Flat (cases, %)	139 (22.7)	10 (16.4)	0 (0)		147 (22.3)	1 (9.1)	1 (20.0)	
Descending (cases, %)	132 (21.5)	9 (14.8)	0 (0)		138 (20.9)	3 (27.3)	0 (0)	
Profound (cases, %)	252 (41.1)	36 (59.0)	2 (100.0)		281 (42.6)	6 (54.5)	3 (60.0)	
Irregular (cases, %)	34 (5.5)	3 (4.9)	0 (0)		35 (5.3)	1 (9.1)	1 (20.0)	
Ascending (cases, %)	56 (9.1)	3 (4.9)	0 (0)		59 (8.9)	0 (0)	0 (0)	

Variables	FT3				FT4			
	Normal	Lower	Higher	*P* value	Normal	Lower	Higher	*P* value
Number (cases, %)	661 (97.78)	4 (0.59)	11 (1.63)		665 (98.37)	7 (1.04)	4 (0.59)	
Age of onset (years)	45.9 ± 15.4	22.5 ± 11.0	23.4 ± 17.3	<0.001	45.7 ± 15.7	30.0 ± 12.4	31.2 ± 4.0	0.006
BMI (kg/m^2)	24.3 ± 3.6	20.7 ± 2.2	22.8 ± 4.5	0.063	24.3 ± 3.6	22.2 ± 3.6	22.6 ± 4.2	0.230
Initial hearing (dB HL)	75.3 ± 32.7	100.0 ± 29.9	86.2 ± 25.4	0.211	75.5 ± 32.8	79.1 ± 22.7	98.4 ± 11.8	0.291
Final hearing (dB HL)	57.6 ± 31.3	80.6 ± 36.5	67.7 ± 31.8	0.170	57.8 ± 31.4	60.9 ± 35.5	70.9 ± 21.1	0.694
Hearing gain (dB HL)	17.8 ± 19.4	19.4 ± 13.8	18.5 ± 24.4	0.809	17.7 ± 19.5	18.2 ± 21.5	27.5 ± 13.8	0.350
Time duration (days)	23.1 ± 25.7	6.8 ± 3.9	25.7 ± 13.5	0.073	23.1 ± 25.6	23.6 ± 23.2	19.0 ± 9.6	0.934
Audiogram type				0.763				0.332
Flat (cases, %)	146 (22.1)	0 (0)	3 (27.3)		148 (22.3)	1 (14.3)	0 (0.0)	
Descending (cases, %)	139 (21.0)	1 (25.0)	1 (9.1)		138 (20.8)	3 (42.9)	0 (0.0)	
Profound (cases, %)	281 (42.5)	3 (75.0)	6 (54.5)		284 (42.7)	2 (28.6)	4 (100.0)	
Irregular (cases, %)	36 (5.4)	0 (0)	1 (9.1)		36 (5.4)	1 (14.3)	0 (0)	
Ascending (cases, %)	59 (8.9)	0 (0)	0 (0)		59 (8.9)	0 (0)	0 (0)	

Variables	TPOA			TGAb		
	Normal	Higher	*P* value	Normal	Higher	*P* value
Number (cases, %)	273 (88.06)	37 (11.94)		282 (90.97)	28 (9.03)	
Age of onset (years)	43.5 ± 16.3	47.5 ± 12.0	0.150	43.7 ± 16.1	46.6 ± 13.2	0.362
BMI (kg/m^2)	24.1 ± 3.9	24.2 ± 3.9	0.881	24.1 ± 3.9	24.3 ± 4.3	0.769
Initial hearing (dB HL)	77.7 ± 33.6	75.8 ± 28.9	0.742	77.9 ± 33.5	73.1 ± 28.5	0.459
Final hearing (dB HL)	59.2 ± 31.8	54.4 ± 30.3	0.381	59.2 ± 31.8	53.2 ± 29.3	0.364
Hearing gain (dB HL)	18.5 ± 20.0	21.5 ± 21.0	0.330	18.7 ± 20.1	19.9 ± 20.1	0.714
Time duration (days)	25.3 ± 26.1	24.6 ± 27.0	0.768	25.3 ± 25.6	24.6 ± 32.4	0.328
Audiogram type			0.629			0.767

(*continued on next page*)

Table 2 (*continued*)

Variables	TPOA			TGAb		
	Normal	Higher	*P* value	Normal	Higher	*P* value
Flat (cases, %)	59 (21.6)	9 (24.3)		61 (21.6)	7 (25.0)	
Descending (cases, %)	46 (16.8)	9 (24.3)		48 (17.0)	7 (25.0)	
Profound (cases, %)	124 (45.4)	16 (43.2)		130 (46.1)	10 (35.7)	
Irregular (cases, %)	18 (6.6)	1 (2.7)		17 (6.0)	2 (7.1)	
Ascending (cases, %)	26 (9.5)	2 (5.4)		26 (9.2)	2 (7.1)	

Continuous variables were presented as mean ± SD for normal distribution, or medians (interquartile range) for non-normal distribution. Categorical variables were presented as *n* (%). All the factors were analyzed by number of persons. TFT: Thyroid functioning testing; TSH: Thyroid stimulating hormone; T4: Thyroxine; T3: Triiodothyronine; FT3: Free triiodothyronine; FT4: Free thyroxine; TPOA: Thyroid peroxidase antibody; TGAb: Thyroglobulin antibodies.

but the PTA.AT was significantly better than non-recovery group. There was statistically difference between both group. This result showed that the hearing level in SSHL is not one of directly influencing factors for the hearing outcome of SSHL. The therapy may be effective if treatment is timely and properly, even if total deafness patients may have good hearing outcome.

In the above contents, we compared and analyzed the results of this study based on previous literatures and the diagnosis and treatment guidelines of SSHL. In addition, we mainly focused on the analysis of thyroid dysfunction in patients with SSHL and the treatment effect of SSHL.

Thyroid hormone (TH) is one of the essential endocrine materials to the development of inner ear function. It can adjust many genes and proteins expression of the auditory pathway. Thyroid hormone deficiency may lead to not only the hearing loss of human and mouse,[11–13] be associated with inner ear diseases, such as Meniere's disease,[14] but also play an important role in the mechanism of deafness caused by *SLC26A4* mutations.[15] In recent years, the proportion of patients with thyroid dysfunction in SSHL has been increasing, which has gradually attracted the attention of otologists. According to one study reported before that the incidence of thyroid dysfunction in SSHL is about 21.6% during the period of 2008 year, significantly higher than the incidence of abnormal thyroid function which was about 10% in the general population.[16,17] Our study revealed a general trend of higher proportion accounted for 24.41%.

The normal function of the thyroid was a positive prognostic factor for hearing recovery in SSHL.[18] Thyroid dysfunction is mainly divided into hyperthyroidism, hypothyroidism, and low T3 syndrome. Among them, hyperthyroidism will lead to increasing of tissue metabolism, blood supply and oxygen consumption, which resulted in the inner ear microcirculation blood supply insufficiency, cochlear blood perfusion decreased, the inner ear blood vessel endothelial cell degeneration necrosis, even the inner ear micro thrombus formation, above these changes may be important mechanisms of hyperthyroidism caused deafness. On the other hand, hypothyroidism can affect not only the inner ear function development, but also can affect the level of blood lipid to promote coronary atherosclerosis, cause high coagulation state, fibrous protein decomposition damage, abnormal function of platelet and endothelial function disorder, also can increase the peripheral vascular resistance and blood pressure levels, make the endothelial dependent vasodilation damage, change the arterial smooth muscle structure, above blood vessels and hemodynamic changes can indirectly lead to hearing loss.[19] Low T3 syndrome is a syndrome with T3 reduction, TSH and T4 normal, which can produce a similar effect of hypothyroidism. It can also affect the function of the auditory system. So, no matter which kind of thyroid dysfunction, or any abnormal thyroid function item may directly or indirectly influence the occurrence, development and treatment effect of deafness. Therefore, we divided all the patients into two groups, abnormal thyroid function group (greater than or equal to 1 item abnormal) and normal thyroid function group. The above grouping helps us to analyze the effect of thyroid dysfunction on SSHL.

Comprehensive statistical analysis results of this study showed that the SSHL onset age of FT3 abnormal group (including low and high group) in patients with SSHL was younger than that in normal FT3 group. The average difference was about 20 years. FT3 is active part of thyroid hormone in blood circulation, is not affected by thyroxine binding globulin, can be truly direct response thyroid function status, the sensitivity and specificity significantly more than T3, has been widely used in clinic. The patients with FT3 change would have the whole thyroid hormone target organs the pathological changes, which lead to it easier for individual patients with SSHL, so that the occurrence of SSHL is in advance or at more younger age. Due to the relatively small sample size of FT3 dysfunction, this results could be further verified by increasing the sample size with our further work.

We also found that the time duration after onset of SSHL in low T3 group was significantly shorter than those in T3 normal group and high T3 group. At the same time, in recovery group of SSHL, the proportion of low T3 was significantly higher than those in non-recovery group, the T3 item was significantly correlated with the effect of SSHL. The simple linear model confirmed that low T3 level was associated with reduced risk of no recovery in SSHL patients. To reveal the true relationship between T3 and the therapeutic effect of SSHL, confounding from age, gender, BMI, pre-treatment hearing and time duration were taken into account, and stratified analysis was conducted. After adjustment, low T3 level was significantly associated with lower odds of non-recovery (*OR* 0.3, 95% *CI* 0.1–0.8) in the

Table 3 Thyroid function profiles according to the outcome of SSHL (cases, %).

Variables[a]	Recovery	Non-recovery	*P* value
Number	303 (44.82)	373 (55.18)	
Thyroid function			0.047
Normal	218 (71.9)	293 (78.6)	
Abnormal (abnormal item $\geq$ 1)	85 (28.1)	80 (21.4)	
TSH			0.615
Normal	272 (89.8)	341 (91.4)	
Low	19 (6.3)	17 (4.6)	
High	12 (4.0)	15 (4.0)	
T3			<0.001
Normal	263 (86.8)	350 (93.8)	
Low	40 (13.2)	21 (5.6)	
High	0 (0)	2 (0.5)	
T4			0.082
Normal	294 (97.0)	366 (98.1)	
Low	8 (2.6)	3 (0.8)	
High	1 (0.3)	4 (1.1)	
FT3			0.525
Normal	298 (98.3)	363 (97.3)	
Low	2 (0.7)	2 (0.5)	
High	3 (1.0)	8 (2.1)	
FT4			0.441
Normal	296 (97.7)	369 (98.9)	
Low	4 (1.3)	3 (0.8)	
High	3 (1.0)	1 (0.3)	
TPOA			0.739
Normal	126 (88.7)	147 (87.5)	
High	16 (11.3)	21 (12.5)	
TGAb			0.743
Normal	130 (91.5)	152 (90.5)	
High	12 (8.5)	16 (9.5)	

[a] All the factors were analyzed by number of persons. TSH: Thyroid stimulating hormone; T4: Thyroxine; T3: Triiodothyronine; FT3: Free triiodothyronine; FT4: Free thyroxine; TPOA: Thyroid peroxidase antibody; TGAb: Thyroglobulin antibodies.

subgroup with longer time duration ($\geq$14 d) compared with the euthyroid cases. The above results mean that low T3 group patients may have the shorter time duration for treatment after onset, which imply effectively hearing outcome of SSHL. And low T3 level has a positive significance for the recovery of SSHL, especially in the group with more than 14 days.

Table 4 The crude and adjusted regression coefficient (β) and 95% confidence interval (*CI*) for hearing outcome in relation to T3 level with and without stratification by time duration.

Group	Crude			Adjusted[a]		
	OR	95%*CI*	*P* value	*OR*	95%*CI*	*P* value
All subjects	0.5	0.3—1.0	0.048	0.7	0.3—1.4	0.267
Time duration						
<14 d	0.6	0.3—1.3	0.233	1.1	0.5—2.4	0.841
$\geq$14 d	0.4	0.1—1.1	0.063	0.3	0.1—0.8	0.019

[a] Adjusted for: age, gender, BMI, pre-treatment hearing, time duration.

T3 is the serum total triiodothyronine, which is one of the most basic screening item for thyroid function. Low T3would reduce the tissue metabolism of the inner ear, liver, kidney, heart, skeletal muscle, etc, and produce similar hypothyroidism role. Through the above hypothyroidism influence on blood vessels and blood rheology to aggravate symptoms of SSHL or ear fullness feeling. The above mechanism may be the cause why the patients with lower T3 had shorter time duration and earlier treatment. Meanwhile, T3 level was related to the therapeutic effect of SSHL in the patients 14 days after the onset of deafness. T3 level may be one of the indicators to evaluate the prognosis of patients with delayed treatment.

According to the grouping of thyroid function normal and abnormal, statistical analysis results showed that age, BMI, PTA-BT, PTA-AT, the hearing improvement, time duration and audiogram types were found no significant difference between the two groups ($P > 0.01$). In addition to the above results, the hearing audiogram type in each item of thyroid function was no statistical difference among groups, which meant that different type of SSHL was no statistical correlation with thyroid function.

Conclusion

In conclusion, we found a higher incidence of thyroid dysfunction in SSHL. There was obvious relationship between T3 and FT3 thyroid dysfunction and the onset time and hearing outcome of SSHL, which indicated that T3 or FT3 indicator may be one of the affecting factors for the prognosis of SSHL. In clinical work, through screening the thyroid function, especial T3 level, may help to evaluate the treatment prognosis of SSHL patients with long time duration.

Declaration of Competing Interest

The authors declare no conflict of interest relevant to this paper.

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References

1. Editorial Board of Chinese Journal of Otorhinolaryngology Head and Neck Surgery; Society of Otorhinolaryngology Head and Neck Surgery, Chinese Medical Association. Guideline of diagnosis and treatment of sudden deafness. *Chin J Otorhinolaryngol Head Neck Surg*. 2015;50:443—447.

2. Kuhn M, Heman-Ackah SE, Shaikh JA, Roehm PC. Sudden sensorineural hearing loss: a review of diagnosis, treatment, and prognosis. *Trends Amplif*. 2011;15:91—105.
3. Bruno R, Aversa T, Catena M, et al. Even in the era of congenital hypothyroidism screening mild and subclinical sensorineural hearing loss remains a relatively common complication of severe congenital hypothyroidism. *Hear Res*. 2015;327:43—47.
4. Li X, Zhang XY, Wang QJ, Wang DY. Efficacy of methylprednisolone sodium succinate for injection (postotic injection) on the auditory threshold and speech recognition rate of sudden deafness patients. *Int J Clin Exp Med*. 2015;8:14110—14114.
5. Nosrati-Zarenoe R, Arlinger S, Hultcrantz E. Idiopathic sudden sensorineural hearing loss: results drawn from the Swedish national database. *Acta Oto-Laryngologica*. 2007;127:1168—1175.
6. Kim JY, Hong JY, Kim DK. Association of sudden sensorineural hearing loss with risk of cardiocerebrovascular disease: a study using data from the Korea National Health Insurance Service. *JAMA Otolaryngol Head Neck Surg*. 2017;21.
7. Becatti M, Marcucci R, Mannucci A, et al. Erythrocyte membrane fluidity alterations in sudden sensorineural hearing loss patients: the role of oxidative stress. *Thromb Haemost*. 2017;117:2334—2345.
8. Chinese Sudden Hearing Loss Multi-center Clinical Study Group. Prospective clinical multi-center study on the treatment of sudden deafness with different typings in China. *Chin J Otorhinolaryngol Head Neck Surg*. 2013;48:355—361.
9. Huy PT, Sauvaget E. Idiopathic sudden sensorineural hearing loss is not an otologic emergency. *Otology & Neurotol-ogy*. 2005;26:896—902.
10. Wang J, Xiao S, Zeng Z, et al. Analyses prognostic factors relevant to sudden sensorineural hearing loss. *Chin J Otorhinolaryngol Head Neck Surg*. 2015;50:448—452.
11. Johnson KR, Gagnon LH, Longo-Guess CM, Harris BS, Chang B. Hearing impairment in hypothyroid dwarf mice caused by mutations of the thyroid peroxidase gene. *J Assoc Res Otolaryngol*. 2014;15:45—55.
12. Overcash RT, Marc-Aurele KL, Hull AD, Ramos GA. Maternal Iodine exposure: a case of fetal goiter and neonatal hearing loss. *Pediatrics*. 2016;137.
13. Lichtenberger-Geslin L, Dos Santos S, Hassani Y, Ecosse E, Van Den Abbeele T, Léger J. Factors associated with hearing impairment in patients with congenital hypothyroidism treated since the neonatal period: a national population-based study. *J Clin Endocrinol Metab*. 2013;98:3644—3652.
14. Santosh UP, Rao MS. Incidence of hypothyroidism in Meniere's disease. *J Clin Diagn Res*. 2016;10:1—3.
15. Dror AA, Lenz DR, Shivatzki S, Cohen K, Ashur-Fabian O, Avraham KB. Atrophic thyroid follicles and inner ear defects reminiscent of cochlear hypothyroidism in Slc26a4-related deafness. *Mamm Genome*. 2014;25:304—316.
16. Oiticica J, Bittar RS. Metabolic disorders prevalence in sudden deafness. *Clinics*. 2010;65:1149—1153.
17. Camargo RY, Tomimori EK, Neves SC, et al. Thyroid and the environment: exposure to excessive nutritional iodine increases the prevalence of thyroid disorders in Sao Paulo, Brazil. *Eur J Endocrinol*. 2008;159:293—299.
18. Narozny W, Kuczkowski J, Kot J, Stankiewicz C, Sicko Z, Mikaszewski B. Prognostic factors in sudden sensorineural hearing loss: our experience and a review of the literature. *Ann Otol Rhinol Laryngol*. 2006;115:553—558.
19. Klein I, Jamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med*. 2001;344:501—509.

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