

Clinical Study on 136 Children with Sudden Sensorineural Hearing Loss

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Abstract

Background: The prevalence of sudden sensorineural hearing loss in children (CSSNHL) is consistently increasing. However, the pathology and prognosis of CSSNHL are still poorly understood. This retrospective study evaluated clinical characteristics and possible associated factors of CSSNHL.

Methods: One hundred and thirty-six CSSNHL patients treated in Department of Otolaryngology-Head and Neck Surgery and Institute of Otolaryngology at Chinese PLA General Hospital between July 2008 and August 2015 were included in this study. These patients were analyzed for clinical characteristics, audiological characteristics, laboratory examinations, and prognostic factors.

Results: Among the 136 patients (151 ears), 121 patients (121 ears, 80.1%) were diagnosed with unilaterally CSSNHL, and 15 patients (30 ears, 19.9%) with bilateral CSSNHL. The complete recovery rate of CSSNHL was 9.3%, and the overall recovery rate was 37.7%. We found that initial degree of hearing loss, onset of treatment, tinnitus, the ascending type audiogram, gender, side of hearing loss, the recorded auditory brainstem response (ABR), and distortion product otoacoustic emissions (DPOAEs) had prognostic significance. Age, ear fullness, and vertigo had no significant correlation with recovery. Furthermore, the relevant blood tests showed 30.8% of the children had abnormal white blood cell (WBC) counts, 22.1% had elevated homocysteine levels, 65.8% had high alkaline phosphatase (ALP), 33.8% had high IgE antibody levels, and 86.1% had positive cytomegalovirus (CMV) IgG antibodies.

Conclusions: CSSNHL commonly occurs unilaterally and results in severe hearing loss. Initial severe hearing loss and bilateral hearing loss are negative prognostic factors for hearing recovery, while positive prognostic factors include tinnitus, gender, the ascending type audiogram, early treatment, identifiable ABR waves, and DPOAEs. Age, vertigo, and ear fullness are not correlated with the recovery. Some serologic indicators, including the level of WBC, platelet, homocysteine, ALP, positive CMV IgG antibody, fibrinogen, and some immunologic indicators, are closely related to CSSNHL.

Key words: Audiological Characteristics; Children; Laboratory Examinations; Prognostic Factors; Sudden Hearing Loss

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined as a hearing loss with a rapid onset in <3 days, and the level of the hearing loss is more than 30 dB in at least three contiguous frequencies.^[1] In the United States, the incidence of SSNHL has been reported to be 27 per 100,000 per year.^[2] Some case studies have shown that SSNHL typically occurs between 46 and 49 years of age.^[3] Studies of SSNHL in children (CSSNHL) are very rare. It has been reported that 6.6% of patients with SSNHL were under 18 years of age,^[4] 3.5% under 14 years,^[5] and only 1.2% under 9 years.^[6]

The pathology of SSNHL remains unclear. However, a series of factors, including viral infections, microcirculatory disorders, autoimmune disorders, and labyrinthine

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hemorrhage, have been proposed as causative factors.^[7-10] In adults, the most possible causes of SSNHL might be microcirculatory disorders,^[11] whereas in children, viral infections could be a crucial causative factor.^[5,12]

In the present study, we systematically analyzed the clinical and audiological characteristics, laboratory examinations, and prognostic factors of 136 Chinese CSSNHL patients.

METHODS

Study design and patients

This retrospective study was performed at Department of Otolaryngology-Head and Neck Surgery and Institute of Otolaryngology at Chinese PLA General Hospital in Beijing. One hundred and thirty-six hospitalized patients (151 ears) between July 2008 and August 2015 in our department have been included in this study. Written informed consents were obtained from all of the patients or their guardians. The study was approved by the Ethics Committee of Chinese PLA General Hospital.

This inclusion criteria of CSSNHL patients were: (1) diagnosed with SSNHL according to the criteria defined in “Clinical Practice Guideline: Sudden Hearing Loss”;^[11] (2) aged between 2 and 18 years; (3) had a complete audiological and other related inspection report; and (4) hospitalized at our department for diagnosis and treatment during the 7-year period from July 2008 to August 2015. Exclusion criteria of CSSNHL patients were: (1) aged under 2 years, because these patients were difficult to distinguish the acquired hearing loss from congenital hearing loss; (2) had ear disorders not related to sudden onset hearing loss, including middle ear disease, retrocochlear disorders, auditory neuropathy, and large vestibular aqueduct syndrome; (3) had systemic diseases; (4) nonorganic hearing loss; or (5) genetic or congenital deafness confirmed by genetic screening or neonatal hearing screening.

All patients underwent a physical examination of the eardrum, and a neurological examination of the cranial nerves III, IV, V, VII, and X. Audiometry was performed with methods most suitable for the age of the patients. Most patients were tested with pure-tone audiometry according to ISO 8253-1. Moreover, tympanometry, auditory brainstem response (ABR), and distortion product otoacoustic emissions (DPOAEs) were performed. The presence of waves I, III, and V of ABR were used in the analysis. The absolute latencies of ABR waves were not analyzed because of the possibility of a latency shift caused by incomplete maturation in children. Young children were tested with behavioral audiometry. Routine blood tests were performed. Viral antibodies against cytomegalovirus (CMV), rubella virus, and herpes simplex virus were detected. Immunological and coagulation examinations were performed.

The hearing thresholds at 0.50, 1.00, 2.00, and 4.00 kHz were measured.^[13] The degrees of hearing loss were categorized as mild (26–40 dB HL), moderate (41–60 dB HL), severe

(61–80 dB HL), and profound hearing loss (>80 dB HL) according to the documentation on prevention of blindness and deafness: Grades of hearing impairment from the World Health Organization. Five types of audiogram configurations were defined based on the pattern of hearing loss: ascending (the average threshold of 0.25–0.50 kHz was 20 dB higher than the median threshold of 4.00–8.00 kHz), descending (the average threshold of 4.00–8.00 kHz was 20 dB higher than the average threshold of 0.25–0.50 kHz), flat (similar threshold observed across the entire frequency range and hearing threshold not exceeding 80 dB HL), profound (similar threshold observed across the entire frequency range and hearing threshold over 80 dB HL), and concave or convex type (average hearing loss on the mid-tone frequency was 20 dB higher than low- and high-frequencies).^[3,4,6,7]

The patients were classified into four groups according to prognosis evaluation: complete recovery, partial recovery, slight recovery, and no-recovery. The complete recovery was defined as pure-tone average <25 dB HL at the final follow-up. The partial recovery was defined as hearing improvement >30 dB. The slight recovery was defined as hearing improvement within 15–30 dB. Patients with hearing recovery <15 dB were included in the no-recovery group. The overall recovery rate was calculated based on patients in complete, partial, and slight recovery groups.^[14]

Treatment

Patients received one or more of the following treatments: low-salt diet, short-term steroid injections, vasodilations, defibrinogenators, plasma expanders, antiviral therapy, anti-inflammatory therapy, the medicines for blood circulation improvement, calcium antagonists, diuretics, and hyperbaric oxygen therapy.^[4,5,7]

Statistical analysis

SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Binary logistic regression analysis, non-parametric Mann–Whitney *U* test, Fisher’s exact test, and Chi-squared test were performed to evaluate clinical characteristics and possible prognostic factors of CSSNHL. Results were considered to be statistically significant when $P < 0.05$. Bonferroni method was used for pair-wise comparisons between multiple samples to adjust the significance level.

RESULTS

Clinical characteristics of patients

Among the 151 ears diagnosed with CSSNHL, 53.0% (80 ears) were from males and 47.0% (71 ears) were from females. The 80.1% (121 ears) were suffered by unilateral loss and 19.9% (30 ears) were bilateral loss. The mean age of all of patients was 11.7 years old (range: 2–18 years). The relevant clinical data are presented in Tables 1 and 2. The time intervals between the onset of CSSNHL, verification of the diagnosis, and treatment varied from 1 day to approximately 183 days (18.5 ± 16.8 days). Most patients received 2 weeks of treatment in the hospital.

Table 1: Characteristics of all CSSNHL based on different hearing loss degrees (N = 151 ears), n (%)

Characteristics	Mild (n = 11)	Moderate (n = 13)	Severe (n = 37)	Profound (n = 90)	Z	P
Unilateral hearing loss	10 (90.9)	12 (92.3)	35 (94.6)	64 (71.1)	-3.178	0.001
Age						
2–6 years	1 (9.1)	0 (0)	4 (10.8)	11 (12.2)	-0.918	0.358
7–12 years	3 (27.3)	7 (53.8)	14 (37.8)	42 (46.7)	-0.866	0.386
13–18 years	7 (63.6)	6 (46.2)	19 (51.4)	37 (41.1)	-1.430	0.153
Accompanying symptoms						
Ear fullness	1 (9.1)	1 (7.7)	7 (18.9)	12 (13.3)	-0.430	0.966
Tinnitus	7 (63.6)	12 (92.3)	33 (89.2)	70 (77.8)	-0.752	0.452
Vertigo	2 (18.2)	6 (46.2)	20 (54.1)	51 (56.7)	-1.727	0.084
Audiogram curve types						
Ascending	5 (45.5)	1 (7.7)	0 (0)	0 (0)	-4.422	0.000
Descending	1 (9.1)	7 (53.8)	6 (16.2)	4 (4.4)	-3.606	0.000
Flat	0 (0)	4 (30.8)	27 (73)	4 (4.4)	-5.022	0.000
Profound	0 (0)	0 (0)	4 (10.8)	82 (91.1)	-10.129	0.000
Concave or convex	5 (45.5)	1 (7.7)	0 (0)	0 (0)	-4.422	0.000

Data were analyzed by non-parametric Mann-Whitney *U* test. CSSNHL: Children sudden sensorineural hearing loss.

Table 2: Characteristics of all CSSNHL based on different age groups (N = 151 ears), n (%)

Characteristics	Age of 2–6 years (n = 16)	Age of 7–12 years (n = 66)	Age of 13–18 years (n = 69)	Statistical values*	P
Male	6 (37.5)	36 (54.5)	38 (55.1)	1.705	0.475
Unilateral hearing loss	8 (50.0)	54 (81.8)	59 (85.5)	10.495	0.005
Accompanying symptoms					
Ear fullness	2 (12.5)	9 (13.6)	10 (14.5)	0.090	1.000
Tinnitus	3 (18.8)	57 (86.4)	62 (89.9)	33.685	0.000
Vertigo	5 (31.3)	34 (51.5)	40 (58.0)	3.681	0.164
Audiogram curve types					
Ascending	1 (6.3)	2 (3.0)	3 (4.3)	0.905	0.714
Descending	0 (0)	9 (13.6)	9 (13.0)	2.184	0.384
Flat	4 (25.0)	12 (18.2)	19 (27.5)	1.764	0.412
Profound	11 (68.8)	40 (60.6)	35 (50.7)	2.294	0.340
Concave or convex	0 (0)	3 (4.5)	3 (4.3)	0.330	1.000
Initial hearing loss					
Mild	1 (6.3)	3 (4.5)	7 (10.1)	1.559	0.487
Moderate	0 (0)	7 (10.6)	6 (8.7)	1.362	0.544
Severe	4 (25.0)	14 (21.2)	19 (27.5)	0.785	0.681
Profound	11 (68.8)	42 (63.6)	37 (53.6)	1.965	0.367

*The Chi-squared test or Fisher's exact test. CSSNHL: Children sudden sensorineural hearing loss.

Audiological characteristic

Of the 151 ears with SSNHL, the hearing loss was characterized as mild in 11 ears (7.3%), moderate in 13 ears (8.6%), severe in 37 ears (24.5%), and profound in 90 ears (59.6%). Among the five defined types of audiogram curves, 6 ears (4.0%) were classified as ascending, 18 ears (11.9%) as descending, 35 ears (23.2%) as flat, 86 ears (57.0%) as profound, and 6 ears (4.0%) as concave or the convex. DPOAEs were performed in 133 ears, among which 22 ears (16.5%) passed, whereas 111 ears (83.5%) failed. For the ABR results performed in 112 ears, waves I, III, and V were evoked and identified in 19 ears (17.0%) and wave V only in 22 ears (19.6%). No ABR-responses can be identified in 71 ears (63.4%). Tympanometry was performed in 140 ears, and 133 ears (95.0%) showed A type curves and 7 ears (5.0%) showed C type curves.

Initial hearing loss in children sudden sensorineural hearing loss

The occurrence of initial degree of hearing loss with respect to side of hearing loss and audiogram curve type differed significantly ($P < 0.05$). The distribution of the initial degree of hearing loss with respect to gender, age, ear fullness, tinnitus, and vertigo did not differ significantly ($P > 0.05$) [Table 1].

Age distribution in children sudden sensorineural hearing loss

Among the 151 ears with SSNHL, 16 ears (10.6%) represented the age group of 2–6 years, 66 ears (43.7%) represented the age group of 7–12 years, and 69 ears (45.7%) represented the age group of 13–18 years.

The distribution of age with regard to side of hearing loss as well as tinnitus was statistically significant ($P < 0.05$). The difference in the distribution of age in relation to gender, ear fullness, vertigo, audiogram curve types, and initial hearing loss showed no statistical significance ($P > 0.05$) [Table 2].

Self-assessed symptoms and possible ethological factors

The 13.9% of patients (21 ears) complained ear fullness, 80.8% of patients (122 ears) reported tinnitus, and 52.3% (79 ears) of patients reported vertigo. Among the 151 ears, 95 ears (63.0%) accompanied with no obvious causative factors, 13 ears (9.0%) with epidemic mumps, 29 ears (19.0%) with upper respiratory infections, 6 ears (4.0%) with fatigue, 5 ears (3.0%) with traumatic injury, and 3 ears (2.0%) with others.

Laboratory examinations of children sudden sensorineural hearing loss

Table 3 shows the number of children with abnormal laboratory tests, including routine blood tests, clinical chemistry examination, virus antibody, immunology examination, and blood coagulation function.

Prognostic factors of children sudden sensorineural hearing loss

The overall recovery rate of children with sensorineural hearing loss was 37.7%. The percentages of patients in complete recovery, partial recovery, slight recovery, and no improvement were 9.3% (14 ears), 9.9% (15 ears), 18.5% (28 ears), and 62.3% (94 ears), respectively.

Multivariate analysis revealed that presence of tinnitus, early treatment, and female had a positive correlation with hearing recovery. Bilateral hearing loss and severe to profound hearing loss had a negative relation to recovery ($P < 0.05$). In univariate analysis, the unilateral, onset of treatment, initial degree of hearing level, the ascending type audiogram, recorded ABR and DPOAEs had statistically significant differences between the recovered and no-recovered groups ($P < 0.05$). The other factors had no significant difference between the recovered and no-recovered groups ($P > 0.05$) [Tables 4 and 5].

DISCUSSION

In this study, 136 patients (151 ears) with CSSNHL were identified, accounting for 8.6% of all patients (1584 cases) with SSNHL who were treated in our department between July 2008 and August 2015. A comparison between SSNHL data and the demographic situation in the referral area showed that the incidence of CSSNHL patients was 10- to 20-fold less than the incidence of SSNHL in adults, which was similar to the study of Chen *et al.*^[15]

Among the 79 cases with viral antibody detection, 68 cases (86.1%) had increased CMV IgG antibody tests. It can be assumed that viral infection is a major cause of CSSNHL.^[4,5,12] Previous studies reported that the main hearing loss caused by CMV infection was severe to

profound, with a fluctuating, progressing, and delayed onset.^[16,17] Worldwide, CMV infection is the most common environmental cause of CSSNHL in very young children, affecting 0.2–2.5% of live-born neonates.^[16] CMV infections include symptomatic infection and asymptomatic infection. Symptomatic infection mostly lead to bilateral hearing loss and asymptomatic infection mainly results in unilateral hearing loss.^[17] According to Karltorp *et al.*,^[18] more than 90% of the CMV-infected children may be asymptomatic. Dried blood spot is used for CMV DNA detection. Thus, this test makes it possible for infected children to diagnose congenital CMV infection. It is also important to make a standard protocol to prevent and treat of CMV.^[18,19]

As shown in Table 1, CSSNHL usually occurred unilaterally (80.1%), which was in line with an earlier study.^[3] Furthermore, bilateral CSSNHL showed a stronger association to profound hearing loss than unilateral CSSNHL. The initial hearing loss was severe in 24.5%, and profound in 59.6%. Regarding to the audiogram patterns, the most common types were flat (23.2%) and profound (57.0%) in conjuncture with severe and profound hearing loss.

There is controversy regarding the age definition of CSSNHL. Some studies used 12 years of age as the threshold,^[17] some used 15 years,^[6] and others used 18 years.^[4,15,20] In this study, we defined a child as the age below 18 years according to the criteria defined in

Table 3: Laboratory examination of all CSSNHL patients in this study

Parameters	Abnormal cases, <i>n</i>	Available cases, <i>n</i>	Ratio (%)
Blood routine			
WBC	41	133	30.8
PLT	40	133	30.1
Blood chemistry determinations			
Triglyceride	11	101	10.9
Cholesterol	13	103	12.6
Homocysteine	17	77	22.0
Total bilirubin	6	116	5.2
ALP	73	111	65.8
Viral antibody detection			
Cytomegalovirus IgG	68	79	86.1
Rubella virus IgG	8	15	53.3
Herpes simplex virus IgG	7	14	50.0
Cytomegalovirus IgM	1	79	1.3
Immunological examination			
IgE	22	65	33.8
IgM	6	65	9.2
IgA	3	65	4.6
IgG	2	65	3.1
Blood coagulation function determination			
D-dimer	20	43	46.5
Fibrinogen	26	96	27.1

CSSNHL: Children sudden sensorineural hearing loss; WBC: White blood cell; PLT: Platelet; ALP: Alkaline phosphatase.

Table 4: Univariate and multivariate analyses of clinical characteristics to hearing recovery in all CSSNHL (N=151 ears), n (%)

Characteristics	Recovery (n = 57)	No recovery (n = 94)	Univariate analysis		Multivariate analysis				
			Statistical values*	P	Wald	P	B	SE	Exp(B)
Male	26 (45.6)	54 (57.4)	1.994	0.180	7.949	0.005	-1.530	0.543	0.217
Age					0.047	0.829			
2–6 years	4 (7.0)	12 (12.8)	1.238	0.414					
7–12 years	22 (38.6)	44 (46.8)	0.973	0.398					
13–18 years	31 (54.4)	38 (40.4)	2.787	0.129					
Unilateral hearing loss	54 (94.7)	67 (71.3)	12.267	0.000	6.848	0.009	1.926	0.736	6.863
Onset of treatment					13.429	0.000	0.107	0.029	1.113
<7 days	26 (45.6)	16 (17.0)	14.448	0.000					
7–14 days	22 (38.6)	19 (20.2)	6.063	0.023					
14–30 days	7 (12.3)	35 (37.2)	11.004	0.001					
>30 days	2 (3.5)	24 (25.5)	12.074	0.000					
Accompanying symptoms									
Vertigo	32 (56.1)	47 (50.0)	0.536	0.504	0.937	0.333			
Tinnitus	50 (87.7)	72 (76.6)	2.829	0.135	4.561	0.033	-1.571	0.736	0.208
Ear fullness	9 (15.8)	12 (12.8)	0.271	0.633	0.109	0.741			

*The Chi-squared test or Fisher's exact test. B: Standardized coefficient; SE: Standard error; CSSNHL: Children sudden sensorineural hearing loss.

Table 5: Univariate and multivariate analyses of audiology characteristics to hearing recovery in all CSSNHL, n (%)

Characteristics	Recovery	No recovery	Univariate analysis		Multivariate analysis				
			Statistical values*	P	Wald	P	B	SE	Exp(B)
Initial degree of hearing loss	n = 57	n = 94			4.757	0.029	0.723	0.331	2.060
Mild	8 (14.0)	3 (3.2)	6.177	0.021					
Moderate	4 (7.0)	9 (9.6)	0.295	0.767					
Severe	19 (33.3)	18 (19.1)	3.859	0.054					
Profound	26 (45.6)	64 (68.1)	6.537	0.010					
Audiogram	n = 57	n = 94			0.710	0.399			
Ascending	5 (8.8)	1 (1.0)	5.525	0.029					
Descending	8 (14.0)	10 (10.6)	0.390	0.607					
Flat	15 (26.3)	20 (21.3)	0.506	0.552					
Profound	27 (47.4)	59 (62.8)	2.832	0.090					
Concave or convex	2 (3.5)	4 (4.3)	0.000	1.000					
ABR	n = 41	n = 71			3.460	0.063			
All waves be evoked	11 (26.8)	8 (11.3)	4.468	0.041					
Only wave V be evoked	8 (19.5)	14 (19.7)	0.000	1.000					
All waves not be evoked	22 (53.7)	49 (69.0)	2.021	0.154					
DPOAE	n = 50	n = 83	5.192	0.023	0.779	0.377			
No evoked	37 (74.0)	74 (89.2)							
Evoked	13 (26.0)	9 (10.8)							

*The Chi-squared test or Fisher's exact test. CSSNHL: Children sudden sensorineural hearing loss; B: Standardized coefficient; SE: standard error; ABR: Auditory brainstem response; DPOAE: Distortion product otoacoustic emission.

“Convention on the Rights of the Child”. As the optimal time for speech and language development in children occurs between 1 and 6 years of age, hearing loss in children can severely affect their speech and cognitive development and increase the burden of society and family. Hormone levels, learning ability, etc., will undergo significant changes during puberty. Similarly, the auditory system will also experience distinct changes.^[21,22] Due to the differences associated with age, the patients in this study were grouped into three groups: 2–6 years, 7–12 years, and 13–18 years. It is not possible to separate CSSNHL from congenital or

progressive hearing loss with certainty in patients under the age of 2 years and is difficult but possible for the age between 2 and 6 years. Since it was important to include young children in the study, especially in studying hearing loss caused by CMV, we included the latter group.

As shown in Table 2, more children expressed tinnitus in the older age groups of 7–12 years and 13–18 years. This was possibly related to the ability of older children to describe their symptoms more clearly. More children occurred unilateral in the older age groups of 7–12 years and 13–18 years. Hence, children in very young age with a

bilateral hearing loss should alert the occurrence of SSNHL. The distribution of age in relation to gender, ear fullness, vertigo, audiogram curve types, and initial degree of hearing loss had no statistical difference.

In our study, immunological examinations were performed on 65 patients. Twenty-two cases (33.8%) showed increased IgE antibodies and six patients (9.2%) showed increased IgM antibodies. Circulating antibodies cross-react with inner ear antigens or activated T-cells, damaging the inner ear.^[23] Therefore, an immunologic mechanism is suspected as a cause of CSSNHL.

Among the 133 patients, 40 patients (30.1%) showed increased platelet (PLT) levels, indicating increased blood coagulation. Promotion of thrombosis may result in a disturbed cochlear microcirculation and an increased risk of CSSNHL. The PLT results may justify further research into the use of thrombolytic drugs in children with SSNHL.^[24] The cochlea receives blood mainly from the labyrinthine artery without shunting vasculature. Cochlear microcirculation is extremely vulnerable to thrombosis, reduced blood flow, and vascular occlusion.^[11] Both disturbance of microcirculation and infection by virus in CSSNHL may cause thrombosis, damage of vessels, and peripheral blood leukocyte effusion. The present study showed that an increased white blood cell (WBC) count had a close relationship with the onset of CSSNHL. Earlier studies have shown that increased numbers of neutrophils and a changed ratio of neutrophils and lymphocytes are negative prognostic factors of SSNHL.^[25-27] In the present study, 133 patients were subjected to a routine blood test, of which 41 patients (30.8%) showed an increased WBC. An increased WBC may be a serological marker of CSSNHL.

In the present study, 77 patients were tested for homocysteine levels, of which 17 patients (22.1%) showed increased values. Homocysteine is an independent risk factor of atherosclerosis and other cardiovascular diseases. It can damage vascular endothelial cells directly or indirectly, promote vascular smooth muscle cell proliferation, effect the oxidation of low-density lipoprotein, strengthen the function of PLT, and promote thrombosis.^[28,29] Accordingly, homocysteine may be a risk factor of CSSNHL.

Some patients showed increased levels of cholesterol (12.6%) and triglyceride (10.9%). Blood lipid metabolic disorders can lead to blood vessel wall lesions, increase blood viscosity, and result in cochlear microcirculation disturbance.^[11,30,31] Thus, elevated blood lipid levels seemed to be related to the CSSNHL. Seventy-three patients (65.8%) showed increased alkaline phosphatase (ALP) levels. Determination of ALP is mainly used for the diagnosis and differential diagnosis of bone, liver, and gallbladder diseases. High-ALP activity is associated with the activity of pluripotent stem cells. ALP activity is increased 1–2 times in children due to bone development. The elevated ALP levels monitored in the present study may be due to physiological development, but correlation with CSSNHL cannot be ruled out.^[32]

Some studies have shown high fibrinogen levels to be a negative prognostic factor of SSNHL. In our study, plasma fibrinogen levels were measured in 96 cases, of which 26 cases (27.1%) exhibited increased levels. Plasma fibrinogen may also be important serological markers of CSSNHL.^[27]

In our study, unilateral hearing loss and early treatment were determined to be positive prognostic factors of hearing recovery. The initial severe hearing loss was shown to be a negative prognostic factor. Tinnitus, ascending type audiogram, gender, identifiable ABR-waves, and DPOAEs were positive prognostic factors regarding hearing recovery in CSSNHL. Age, vertigo, and ear fullness were found to be independent of recovery. The presence of vertigo is widely used to indicate poor recovery in CSSNHL.^[3] In the present study, patients with sudden hearing loss accompanied by vertigo accounted for 52.3% of all subjects, with no significant correlation with recovery. The relationship between tinnitus and recovery remains a debated topic. Some studies suggested that tinnitus is an important positive prognostic factor of CSSNHL,^[4] while other studies showed independence.^[3] In the present study, 80.8% of patients reported tinnitus, with a partial or total recovery rate of 33.1%. The presence of tinnitus was determined to be a positive factor associated with hearing recovery in CSSNHL according to the multivariate analysis, but was determined to be unrelated according to univariate analysis.

The difference between the results of the multivariate analysis and the univariate analysis with regard to gender, tinnitus, audiogram, ABR, and DPOAEs may be related to a combined effect. Further study of these potential factors is required. The complex pathogenesis of CSSNHL, the poor expression ability of children, and the retrospective nature of this study all limited the significance of this study.

In conclusion, CSSNHL predominantly occurs unilaterally and is in conjunction with severe hearing loss. In our study, complete recovery was observed in 9.3% of patients, and overall recovery rate was 37.7%. Initial severe hearing loss and bilateral hearing loss were negative prognostic factors for hearing recovery. Age, vertigo, and ear fullness were irrelevant to the prognosis. Tinnitus, gender, ascending type audiogram, identifiable ABR-waves, and DPOAEs were positive prognostic factors for hearing recovery. We also found that the level of WBC, PLT, homocysteine, ALP, positive CMV IgG antibody, fibrinogen, and some immunologic indicators were closely related to CSSNHL. These findings support that several important clinical indicators benefit the diagnosis and treatment of CSSNHL.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Stachler RJ, Chandrasekhar SS, Archer SM, Rosenfeld RM, Schwartz SR, Barrs DM, *et al.* Clinical practice guideline: Sudden hearing loss. *Otolaryngol Head Neck Surg* 2012;146 3 Suppl:S1-35. doi: 10.1177/0194599812436449.
2. Alexander TH, Harris JP. Incidence of sudden sensorineural hearing loss. *Otol Neurotol* 2013;34:1586-9. doi: 10.1097/MAO.0000000000000222.
3. Roman S, Aladio P, Paris J, Nicollas R, Triglia JM. Prognostic factors of sudden hearing loss in children. *Int J Pediatr Otorhinolaryngol* 2001;61:17-21. doi: 10.1016/S0165-5876(01)00538-9.
4. Chung JH, Cho SH, Jeong JH, Park CW, Lee SH. Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss in children. *Laryngoscope* 2015;125:2209-15. doi: 10.1002/lary.25196.
5. Jecmenica J, Bajec-Opancina A. Sudden hearing loss in children. *Clin Pediatr (Phila)* 2014;53:874-8. doi: 10.1177/0009922814533402.
6. Na SY, Kim MG, Hong SM, Chung JH, Kang HM, Yeo SG. Comparison of sudden deafness in adults and children. *Clin Exp Otorhinolaryngol* 2014;7:165-9. doi: 10.3342/ceo.2014.7.3.165.
7. Lee HS, Lee YJ, Kang BS, Lee BD, Lee JS. A clinical analysis of sudden sensorineural hearing loss cases. *Korean J Audiol* 2014;18:69-75. doi: 10.7874/kja.2014.18.2.69.
8. Cohen BE, Durstenfeld A, Roehm PC. Viral causes of hearing loss: A review for hearing health professionals. *Trends Hear* 2014;18. pii: 2331216514541361. doi: 10.1177/2331216514541361.
9. Salomone R, Abu TA, Chaves AG, Bocalini MC, Vicente Ade O, Riskalla PE. Sudden hearing loss caused by labyrinthine hemorrhage. *Braz J Otorhinolaryngol* 2008;74:776-9. doi: 10.1016/S1808-8694(15)31390-2.
10. 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. doi: 10.1177/10847138111408349.
11. Lu YY, Jin Z, Tong BS, Yang JM, Liu YH, Duan M. A clinical study of microcirculatory disturbance in Chinese patients with sudden deafness. *Acta Otolaryngol* 2008;128:1168-72. doi: 10.1080/00016480801901626.
12. Zhang X, Xu X, Ma W, Zhang Q, Tong B, Yu H, *et al.* A clinical study of sudden deafness. *Acta Otolaryngol* 2015;135:1030-5. doi: 10.3109/00016489.2015.1060629.
13. Wang M, Han Y, Fan Z, Zhang D, Wang H. Therapeutic effect on idiopathic sudden sensorineural hearing loss with duration of onset more than 3 months. *Indian J Otolaryngol Head Neck Surg* 2013;65:61-5. doi: 10.1007/s12070-012-0604-8.
14. Wang DY, Hou ZQ, Liu Y, Gao Y, Zhao FF, Zong L, *et al.* Clinical and prognostic analyses of juvenile sudden sensorineural hearing loss (in Chinese). *Nati Med J China* 2013;93:1574-6. doi: 10.3760/cma.j.issn.0376-2491.2013.20.016.
15. Chen YS, Emmerling O, Ilgner J, Westhofen M. Idiopathic sudden sensorineural hearing loss in children. *Int J Pediatr Otorhinolaryngol* 2005;69:817-21. doi: 10.1016/j.ijporl.2005.01.015.
16. Goderis J, De Leenheer E, Smets K, Van Hoecke H, Keymeulen A, Dhooge I. Hearing loss and congenital CMV infection: A systematic review. *Pediatrics* 2014;134:972-82. doi: 10.1542/peds.2014-1173.
17. Furutate S, Iwasaki S, Nishio SY, Moteki H, Usami S. Clinical profile of hearing loss in children with congenital cytomegalovirus (CMV) infection: CMV DNA diagnosis using preserved umbilical cord. *Acta Otolaryngol* 2011;131:976-82. doi: 10.3109/00016489.2011.583268.
18. Karltorp E, Hellström S, Lewensohn-Fuchs I, Carlsson-Hansén E, Carlsson PI, Engman ML. Congenital cytomegalovirus infection – A common cause of hearing loss of unknown aetiology. *Acta Paediatr* 2012;101:e357-62. doi: 10.1111/j.1651-2227.2012.02711.x.
19. Engman ML, Malm G, Engstrom L, Petersson K, Karltorp E, Tear Fahnehjelm K, *et al.* Congenital CMV infection: Prevalence in newborns and the impact on hearing deficit. *Scand J Infect Dis* 2008;40:935-42. doi: 10.1080/00365540802308431.
20. Morita S, Suzuki M, Iizuka K. Non-organic hearing loss in childhood. *Int J Pediatr Otorhinolaryngol* 2010;74:441-6. doi: 10.1016/j.ijporl.2010.01.003.
21. Welch D, Dawes PJ. Childhood hearing is associated with growth rates in infancy and adolescence. *Pediatr Res* 2007;62:495-8. doi: 10.1203/PDR.0b013e3181425869.
22. Al-Mana D, Ceranic B, Djahanbakhch O, Luxon LM. Hormones and the auditory system: A review of physiology and pathophysiology. *Neuroscience* 2008;153:881-900. doi: 10.1016/j.neuroscience.2008.02.077.
23. Greco A, Fusconi M, Gallo A, Marinelli C, Macri GF, De Vincentiis M. Sudden sensorineural hearing loss: An autoimmune disease? *Autoimmun Rev* 2011;10:756-61. doi: 10.1016/j.autrev.2011.05.005.
24. Karli R, Alacam H, Unal R, Kucuk H, Aksoy A, Ayhan E. Mean platelet volume: Is it a predictive parameter in the diagnosis of sudden sensorineural hearing loss? *Indian J Otolaryngol Head Neck Surg* 2013;65:350-3. doi: 10.1007/s12070-013-0648-4.
25. Masuda M, Kanzaki S, Minami S, Kikuchi J, Kanzaki J, Sato H, *et al.* Correlations of inflammatory biomarkers with the onset and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2012;33:1142-50. doi: 10.1097/MAO.0b013e3182635417.
26. Seo YJ, Jeong JH, Choi JY, Moon IS. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio: Novel markers for diagnosis and prognosis in patients with idiopathic sudden sensorineural hearing loss. *Dis Markers* 2014;2014:702807. doi: 10.1155/2014/702807.
27. Kanzaki S, Sakagami M, Hosoi H, Murakami S, Ogawa K. High fibrinogen in peripheral blood correlates with poorer hearing recovery in idiopathic sudden sensorineural hearing loss. *PLoS One* 2014;9:e104680. doi: 10.1371/journal.pone.0104680.
28. Passamonti SM, Di Bernardino F, Bucciarelli P, Berto V, Artoni A, Gianniello F, *et al.* Risk factors for idiopathic sudden sensorineural hearing loss and their association with clinical outcome. *Thromb Res* 2015;135:508-12. doi: 10.1016/j.thromres.2015.01.001.
29. Fusconi M, Chistolini A, de Virgilio A, Greco A, Massaro F, Turchetta R, *et al.* Sudden sensorineural hearing loss: A vascular cause? Analysis of prothrombotic risk factors in head and neck. *Int J Audiol* 2012;51:800-5. doi: 10.3109/14992027.2012.705904.
30. Capaccio P, Ottaviani F, Cuccharini V, Bottero A, Schindler A, Cesana BM, *et al.* Genetic and acquired prothrombotic risk factors and sudden hearing loss. *Laryngoscope* 2007;117:547-51. doi: 10.1097/MLG.0b013e31802f3c6a.
31. Aimoni C, Bianchini C, Borin M, Ciorba A, Fellin R, Martini A, *et al.* Diabetes, cardiovascular risk factors and idiopathic sudden sensorineural hearing loss: A case-control study. *Audiol Neurootol* 2010;15:111-5. doi: 10.1159/000231636.
32. Štefková K, Procházková J, Pacherník J. Alkaline phosphatase in stem cells. *Stem Cells Int* 2015;2015:628368. doi: 10.1155/2015/628368.