

ORIGINAL RESEARCH

Clinical features and hearing prognosis of idiopathic sudden sensorineural hearing loss in patients undergoing hemodialysis: A retrospective study

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Funding information

JSPS KAKENHI, Grant/Award Number: 20K18263

Abstract

Background: Patients undergoing hemodialysis (HD) tend to experience hearing loss, including idiopathic sudden sensorineural hearing loss (ISSHL). However, little is known about the relationship between HD and ISSHL.

Objective: To investigate the effects of HD on the hearing level and the treatment prognosis of ISSHL.

Methods: We reviewed the medical records of 23 patients with ISSHL receiving HD treatment (HD group) and 101 patients with ISSHL not receiving HD treatment (non-HD group), and assessed clinical features, results of audiometric tests and blood examination results.

Results: Statistically significant differences were not observed in pretreatment hearing level and hearing recovery of the ear affected with ISSHL between the two groups ($P > .05$). Conversely, hearing thresholds in the unaffected ear were statistically different ($P < .0001$), and the hearing thresholds of the HD groups were significantly increased compared with those of the non-HD groups, especially at high frequency. In addition, patients with renal dysfunction not receiving HD treatment showed similar hearing thresholds in the unaffected ear when compared with patients receiving HD treatment.

Conclusion: HD itself did not influence the treatment prognosis of ISSHL. Renal dysfunction itself, and not HD treatment, worsened the hearing level. As similar treatment results are expected, standard treatment should be administered to patients undergoing HD.

Level of Evidence: 3b.

KEYWORDS

hearing prognosis, hemodialysis, idiopathic sudden sensorineural hearing loss

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1 | INTRODUCTION

The pathogenesis of idiopathic sudden sensorineural hearing loss (ISSHL) has been attributed to microcirculation disorders, viral infection, autoimmune diseases, and so on.¹ However, the cause of ISSHL remains unclear. Accordingly, the optimal treatment modality for ISSHL is still controversial. Among various comprehensive approaches, combination therapy comprising topical systemic steroids and vasodilator drugs has been used as the primary treatment.² However, despite comprehensive treatment with systemic steroids, the spontaneous recovery rate ranges from only 30% to 60%.³

It has been reported that hearing loss (HL) often coexists in patients undergoing hemodialysis (HD), with 20% to 75% of them suffering from a hearing problem.^{4,5} Etiologic agents of HL in patients undergoing HD are presumed, such as a drastic change in plasma osmolality, antigen similarity between the renal glomerulus and labyrinth of the inner ear, compromised immune system against virus infection, and so on.⁶ Other study revealed chronic kidney disease itself was associated with HL.⁷ Patients with chronic renal failure (CRF) or end-stage kidney disease tend to experience ISSHL more frequently because of a drastic change in hemodynamics caused by HD.^{4,5} By contrast, a previous study demonstrated that HD itself did not affect the hearing prognosis of patients with ISSHL.⁸ Therefore, the relationship between ISSHL and HD has not been fully elucidated. Consequently, the effect of global standard treatment, such as systemic steroid therapy for patients undergoing HD, is uncertain. In this study, we compared 23 patients with ISSHL who required HD and 101 patients with ISSHL who did not to investigate the effect of HD treatment on hearing disorders, including ISSHL.

2 | METHODS

2.1 | Research design

This retrospective study was approved by the Institutional Review Board of Kitasato University Hospital (B20-056) and Kitasato University Medical Center (2021004). Because of the retrospective nature of the study, the need for informed consent was waived.

2.2 | Patients

We retrospectively reviewed the medical records of patients with ISSHL who required HD between 2007 and 2020 in Kitasato University Hospital and Kitasato University Medical Center Hospital (HD group) and those who did not require HD between 2017 and 2018 (non-HD group). The inclusion criteria for ISSHL were as follows: (a) sudden sensorineural HL of 30 dB or greater in at least three consecutive frequencies; (b) early therapeutic management, that is, treatment initiated within 2 weeks after onset; (c) age over 18 years. In the non-HD group, we primarily judged the need for hospitalization based on symptoms, such as dizziness or a history of diabetes mellitus

(DM), whereas in the HD group, patients who agreed to receive systemic steroid therapy were basically hospitalized regardless of the associated symptoms. We excluded patients with any history of genetic or fluctuating HL or otologic surgery.

2.3 | Hearing test

Pure-tone audiometry was performed using a conventional device (AA-78; Rion, Tokyo, Japan) in a soundproof room. First, the hearing thresholds were obtained through air conduction at frequencies of 0.125, 0.25, 0.5, 1, 2, 4, and 8 kHz and bone conduction at frequencies of 0.25 to 4 kHz for both ears. The arithmetic average air conduction thresholds were calculated from the thresholds at 0.25, 0.5, 1, 2, and 4 kHz. The HL grade, defined according to the guidelines of the Japanese Ministry of Health and Welfare, was then determined using the initial audiogram data. Hearing recovery was calculated as the difference between the average hearing thresholds at different time points, including the initial day of treatment and more than 3 months after initial treatment. The evaluation of hearing recovery was based on the hearing outcome criteria proposed by the Acute Severe Hearing Loss Study Group of the Ministry of Health, Labor, and Welfare of Japan (Table 1), and patients were accordingly classified into the following two groups: the good prognosis group (ie, complete and marked recovery) and the poor prognosis group (ie, slight and no recovery).

2.4 | Treatment

As a standard treatment, we administered a 10-day course of systemic corticosteroids (8 mg betamethasone via intramuscular injection for the first day followed by 4 mg betamethasone via oral administration for the first 3 days, tapered to 2 mg for the second 3 days and 1 mg for the last 3 days). To enhance the efficacy of treatment, combination therapy with systemic corticosteroid administration, intratympanic steroid injection, or systemic prostaglandin E1 (vasodilator) application was used in some cases (Table S1).

TABLE 1 Final treatment outcomes according to the guideline of the Acute Severe Hearing Loss Study Group of the Ministry of Health, Labor, and Welfare of Japan

Description	n (%)	
Complete recovery: CR	All five frequencies at 0.25, 0.5, 1, 2, and 4 kHz of final audiograms are 20 dB or less, or improvement to the same degree of hearing in the unaffected ear	31 (25.0%)
Marked recovery: MR	30 dB ≤ PTA improvement	37 (29.8%)
Slight recovery: SR	10 dB ≤ PTA improvement < 30 dB	31 (25.0%)
No recovery: NR	PTA improvement < 10 dB	25 (20.2%)

Abbreviation: PTA, pure-tone audiometry.

2.5 | Assessment

We investigated individual clinical features and examination results, including age at onset, laterality, vertigo, time from the onset to the start of treatment, pretreatment hearing thresholds, hearing recovery, intratympanic steroid administration, and blood-sampling results (creatinine [Cr], estimated glomerular filtration rate [eGFR], hemoglobin [Hb], hemoglobin A1c [HbA1c]). Renal dysfunction (RD) was defined as eGFR <60 mL/minute.⁷

2.6 | Statistical analyses

Statistical analysis was conducted using GraphPad Prism 8 (GraphPad Software Inc., La Jolla, California) or JMP 14.2 (SAS Institute Japan Inc., Tokyo, Japan). We used the chi-squared test to evaluate the clinical characteristics and possible prognostic factors. We applied the *t* test or nonparametric Mann-Whitney *U* test to investigate continuous variable prognostic factors. We analyzed the difference in hearing thresholds using a two-way analysis of variance (ANOVA) followed by Šidák's multiple comparisons test. A *P* value of <.05 was considered statistically significant.

3 | RESULTS

3.1 | Clinical features

A total of 124 patients (HD group: *n* = 23; non-HD group: *n* = 101) were included in this study. Table 2 presents the clinical features of patients in the HD and non-HD groups. There was no significant difference between the two groups with respect to age, side of the affected ear, dizziness, days from the onset to the start of treatment,

intratympanic steroid therapy, or recovery outcome. The HD group included a statistically higher number of patients with DM (*P* < .05). In the HD group, HD was introduced because of DM in 16 cases (70%), drug-induced interstitial nephritis in one case (4%), membranous nephropathy in one case (4%), and unknown in five cases (22%). Next, we investigated the hematologic examination related to renal functions. We observed a statistically significant difference in Cr and eGFR values in the blood examination (*P* < .05; Table 2). Additionally, Hb was also found to be statistically different between the two groups (HD group: 11.7 ± 0.7 g/dL, non-HD group: 13.8 ± 0.3 g/dL) because of renal anemia, which was attributed to the lack of erythropoietin (*P* < .05). Although the HD group included more patients with DM, a statistically significant difference was not observed in HbA1c score.

3.2 | Hearing prognosis

Figure 1 shows the hearing results in the affected ear, as measured by pure-tone audiometry. Statistical significance was not observed in all frequencies of the pretreatment hearing thresholds between the two groups (two-way ANOVA followed by Šidák's multiple comparisons test, 0.125 kHz, *P* = .99; 0.25 kHz, *P* = .92; 0.5 kHz, *P* = .37; 1 kHz, *P* = .23; 2 kHz, *P* = .31; 4 kHz, *P* = .35; 8 kHz, *P* = .64; Figure 1A). Additionally, the average hearing thresholds also showed no statistically significant differences between the two groups in pretreatment (Mann-Whitney *U* test, *P* = .12; Figure 1B). Furthermore, the thresholds recovery was not statistically significantly different between the HD and non-HD groups at all frequencies (two-way ANOVA, *P* = .98; Figure 1C). These data indicated that the treatment effects for ISSHL in patients undergoing HD were comparable with those not receiving HD.

We further investigated the hearing status in the unaffected ear. Hearing thresholds in the unaffected ear were significantly different

Variables	HD (n = 23)	Non-HD (n = 101)	<i>P</i>
Age (year)	64.7 ± 1.8	61.5 ± 1.5	.33
Affected side (right/left)	12/11	46/55	.57
Diabetes mellitus (+/−)	16/7	31/70	.0005***
Severity grade (1/2/3/4)	0/4/10/9	16/14/40/31	.23
Dizziness (+/−)	7/16	32/69	.91
Onset to the start of treatment (days)	5.0 ± 0.7	5.4 ± 0.4	.70
Intratympanic therapy (+/−)	8/15	28/73	.50
Outcome (CR/MR/SR/NR)	3/9/7/4	28/28/24/21	.41
Blood examination			
Cr (mg/dL)	8.4 ± 0.6	0.8 ± 0.01	<.0001****
eGFR (mL/min)	7.5 ± 1.9	70.0 ± 2.0	<.0001****
Hb (g/dL)	11.6 ± 0.3	13.8 ± 0.2	<.0001****
HbA1c (%)	6.7 ± 0.4	6.2 ± 0.1	.09

TABLE 2 Clinical features and treatment outcomes

Abbreviations: Cr, creatinine; CR, complete recovery; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HbA1c, hemoglobin A1c; HD, hemodialysis; MR, marked recovery; non-HD, non-hemodialysis; NR, no recovery; SR, slight recovery.

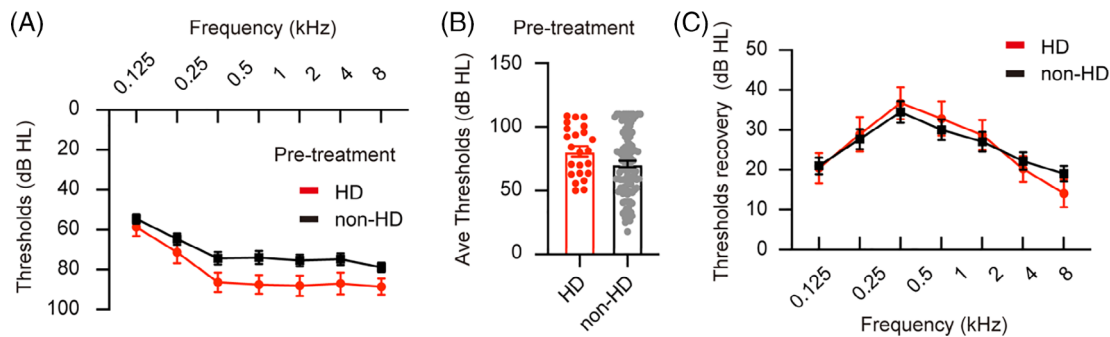


FIGURE 1 Treatment outcomes of hearing thresholds in the affected ear. A, Pretreatment hearing thresholds were not statistically significantly different between the HD and non-HD groups. B, Average hearing thresholds were not statistically significantly different between the HD and non-HD groups. C, The thresholds recovery was not statistically significantly different between the HD and non-HD groups at all frequencies. HD, hemodialysis; non-HD, non-hemodialysis

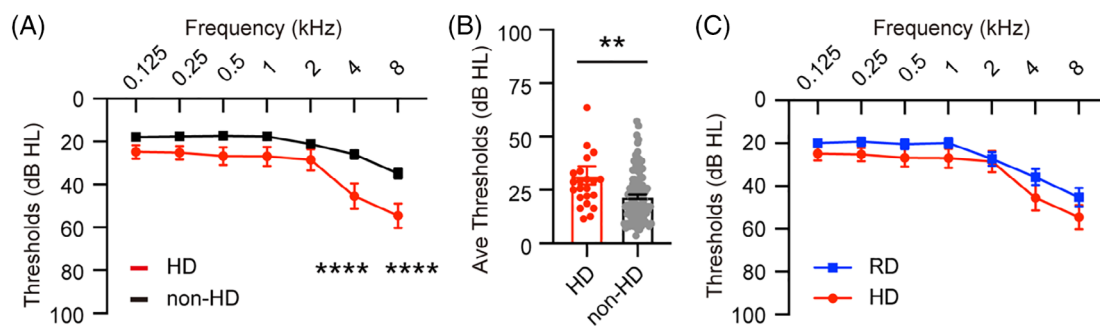


FIGURE 2 Hearing status in the unaffected ear. A, Pretreatment hearing thresholds were statistically significantly different between the HD and non-HD groups at 4 and 8 kHz. B, Average hearing thresholds were statistically significantly different between the HD and non-HD groups. C, No statistically significant difference was observed in the unaffected ear between the HD and RD groups. ** $P < .01$; **** $P < .0001$. HD, hemodialysis; non-HD, non-hemodialysis; RD, renal dysfunction

TABLE 3 Prognostic factors for ISSHL

Variables	Good prognosis (n = 68)	Poor prognosis (n = 56)	P
Age (year)	61.6 ± 1.8	62.7 ± 1.7	.68
Affected side (right/left)	34/34	24/32	.43
Average hearing level	73.1 ± 3.0	72.2 ± 3.5	.83
Onset to the start of treatment (days)	5.7 ± 0.6	5.0 ± 0.4	.39
Diabetes mellitus (+/-)	26/42	21/35	.93
Hemodialysis (+/-)	12/56	11/45	.78
Intratympanic therapy (+/-)	15/53	21/35	.06
Blood examination			
Cr (mg/dL)	2.4 ± 0.4	2.1 ± 0.4	.66
eGFR (mL/min)	57.8 ± 3.8	59.2 ± 4.1	.81
Hb (g/dL)	13.4 ± 0.2	13.4 ± 0.3	.93
HbA1c (%)	6.3 ± 0.1	6.3 ± 0.2	.90

Abbreviations: Cr, creatinine; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HbA1c, hemoglobin A1c.

between the two groups (two-way ANOVA, $P < .0001$; Šidák's multiple comparison test, 0.125 kHz, $P = .38$; 0.25 kHz, $P = .27$; 0.5 kHz, $P = .08$; 1 kHz, $P = .08$; 2 kHz, $P = .32$; 4 kHz, $P < .0001$; 8 kHz, $P < .0001$; Figure 2A). Furthermore, there was a statistically significant

difference in average hearing thresholds between the two groups (HD group: 31.8 ± 4.3 dB, non-HD group: 21.9 ± 1.2 dB; Mann-Whitney U test, $P = .005$; Figure 2B). These data indicated that HD treatment itself or the reasons for the need of HD, such as RD, might

affect hearing level in the unaffected ears. Therefore, to further elucidate the effects of HD itself, not but RD, on the hearing level in the unaffected ears, we compared the hearing level of HD and RD groups. The non-HD patients were further divided into two groups of the normal renal function (eGFR \geq 60: $n = 75$) and the renal dysfunction groups (RD group; eGFR $<$ 60: $n = 26$). Table S2 presents the clinical features of patients in the HD and RD groups. There was no significant difference between the two groups with respect to age, side of the affected ear, dizziness, days from the onset to the start of treatment, intratympanic steroid therapy, or recovery outcome. Hearing thresholds in the unaffected ear were not statistically different between the HD and RD groups (Figure 2C). Our results indicated that HD itself does not affect the hearing level in the unaffected ears, that is, RD could influence the hearing level.

3.3 | Prognostic factors

Finally, we investigated the prognostic factors of ISSHL. All patients were categorized in the good prognosis group (complete and marked recovery: $n = 68$) and the poor prognosis group (slight and no recovery: $n = 56$) regardless of the need of HD. We compared the various factors, including HD treatment and renal function, between the groups. No factors showed a statistically significant difference between the groups with a good and poor prognosis (Table 3), indicating that HD treatment itself, and renal function did not affect the prognosis of ISSHL.

4 | DISCUSSION

Reports focusing on HL in patients undergoing HD are limited, and the assessment of the relationship between HD and HL is not yet concrete. In this study, we investigated the effect of HD treatment on the hearing prognosis of patients with ISSHL. We found no significant difference between the HD and non-HD groups in ISSHL treatment outcome as well as in clinical features such as age, initial hearing level, and so on. Although the HD group included more patients with DM, the outcome was similar, and we observed a hearing recovery of approximately 25 dB in both groups after initial treatment. These results suggest that HD itself might not affect the treatment outcome of ISSHL so much. Our results are consistent with those of a previous report that demonstrated that patients with ISSHL undergoing HD did not have a worse hearing prognosis.⁸

As the results of our study indicate that HD does not interfere with the treatment outcomes of ISSHL, standard treatment, using mainly corticosteroid tapering and vasodilators, should be conducted in patients undergoing HD in the same way as in those not receiving it. Moreover, because the pharmacokinetics of the administered corticosteroid is considered independent of HD, the amount of steroid should not be adjusted by renal function.⁹ However, depending on the general condition of the patient, systemic corticosteroid administration should be tapered, refrained, or changed to intratympanic

injection. In our study, systemic corticosteroid therapy was suspended in one patient undergoing HD because of gastrointestinal bleeding. Except for this one patient, no other complications were seen in either group.

A previous study reported that 15 of 28 patients undergoing HD showed high-frequency HL and that HL was correlated with the duration of HD.⁷ Another study revealed that transient hearing fluctuation was seen at >2 kHz in 61 patients with CRF, independent of blood glucose level, blood pressure, body weight, and blood concentration of sodium, potassium, calcium, and urea nitrogen.⁴ Furthermore, a prior study reported elevated hearing thresholds in the nonaffected ear in HD patients.⁹ Consistent with these reports, we found that the hearing thresholds in the unaffected ear at the first visit were elevated at 4 kHz and 8 kHz in the HD group, although no statistical significance was noted in the hearing level of the affected side. These results indicate that the HD treatment itself or the etiology leading to HD treatment might affect the increase in hearing thresholds in the unaffected ear. We further compared the hearing level of HD and RD groups to investigate the factors that cause HL. This comparison suggested that RD affects the hearing level, but HD does not do so. Some studies have reported that low eGFR, that is, weakened kidney function is associated with HL, similar to the results of our study.^{10,11} Although the inner ear and kidney have structural similarities, the etiology of an association between kidney function and hearing level is uncertain. In the HD and RD group, the elevation in the hearing threshold of the unaffected side might reflect microangiopathy due to ischemic inner ear damages caused by RD. Consistent with this, in cohort studies focusing on patients undergoing HD, a cardiovascular event occurred more frequently in patients with ISSHL.^{5,12} The findings of our study have important clinical implications for the understanding and management of patients with ISSHL undergoing HD.

Nevertheless, our study has several limitations. One limitation is that the HD group included more patients with DM than the control group did, and DM itself might affect hearing status. The second limitation is that this was a retrospective study conducted in two hospitals, and the sample size was relatively small. Thus, to validate our findings, further prospective studies that include larger populations are needed.

5 | CONCLUSION

We reviewed the treatment outcome and hearing status in patients with ISSHL undergoing HD and compared them with those of the patients with ISSHL not receiving HD. Although the treatment outcome in the affected ear was not statistically different between the groups, the hearing threshold was elevated at high frequency in the nonaffected ears in the HD group. Hearing thresholds in the unaffected ear are not statistically different between the HD and RD groups. These results indicate that the causes of HD, such as DM or CRF, can affect hearing level. As similar treatment outcomes were expected, patients undergoing HD should be treated with systemic steroids.

ACKNOWLEDGMENT

This work was supported by JSPS KAKENHI grant (grant number 20K18263).

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Yamamoto K, Kurioka T, Furuki S, et al. Clinical features and hearing prognosis of idiopathic sudden sensorineural hearing loss in patients undergoing hemodialysis: A retrospective study. *Laryngoscope Investigative Otolaryngology*. 2021;6(5):1104-1109. <https://doi.org/10.1002/lio2.630>