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Original Article

Discriminant Analysis of the Prognostic Factors for Hearing Outcomes in Patients with Idiopathic Sudden Sensorineural Hearing Loss

Ahmed Attia Askar[1], Mohamed Rashad Ghonim[2], Yousef Kamel Shabana[2]

[1]Student Hospital, Mansoura University, Mansoura, Egypt
[2]Department of Otorhinolaryngology, Mansoura University, Faculty of Medicine, Mansoura, Egypt

ORCID iDs of the authors: A.A.A. 0009-0006-2658-1044, M.R.G. 0000-0003-0875-2920, Y.K.S. 0000-0002-6114-3625.

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BACKGROUND: This study aims to determine and assess prognostic variables that might affect the hearing result in patients with idiopathic sudden sensorineural hearing loss following intratympanic steroid injection.

METHODS: In total, 190 patients with idiopathic sudden sensorineural hearing loss received intratympanic steroid injection. Two hearing indices (recovery and nonrecovery) will be analyzed as dependent variables; patient's age, time period between the onset of hearing loss and treatment, initial level of hearing (hearing loss pre), type of audiogram curve (upsloping, downsloping, and flat), presence of vertigo, presence of tinnitus, and diabetes) will be analyzed as prognostic factor variables.

RESULTS: Recovery was seen in 72% of the patients. Different preinjection audiogram curves and hearing grades had a significant effect on recovery, absence of vestibular symptoms and no diabetic history were noted to have a good prognosis. Delay in treatment by more than 30 days from the onset of hearing loss was associated with a worse prognosis.

CONCLUSION: Idiopathic sudden sensorineural hearing loss associated with late treatment plan more than 1 month, presence of vertigo, diabetes, and profound prehearing loss were negative prognostic factors. Whereas age, gender, and presence of tinnitus did not affect prognosis. More stable response was obtained when intratympanic steroids were added within 1 month after diagnosis, and the patient presented with mild or moderate hearing loss grade, flat or downsloping pure tone audiometery curve, and absence of vertigo and nondiabetic with significantly good results.

KEYWORDS: Sudden sensorineural hearing loss, discriminant analysis, intratympanic injection

INTRODUCTION

The most often mentioned causes of sudden sensorineural hearing loss (HL) include infection with the virus, thromboembolic vascular dysfunction, and immunologic abnormalities. Numerous approaches, such as vasodilators, anticoagulants, anti-inflammatory medications, diuretics, and hyperbaric oxygen treatment, have been suggested to manage nonapproved protocols. The characteristic symptom of idiopathic sudden sensorineural hearing loss (ISSNHL) is abrupt unilateral deafness with a rapid onset of more than 30 dB HL at 3 consequential frequencies over the course of 3 days.[1]

Steroid therapy is nowadays the most accepted management for ISSNHL despite the debates surrounding its medical care; nonetheless, the large dose needed for systemic therapy can result in both early and late complications.[2]

Within 2 weeks after the commencement, there was a 30% likelihood of spontaneous recovery without known conventional treatment.[3]

Intratympanic steroid (ITS) is able to treat an organ specifically and avoid the side effects of systemic corticosteroid therapy by administering large dosages of medication directly via mesotympanum across the membrane of the round window.[4]

Corresponding author: Ahmed Mohamed Ahmed Attia, e-mail: egoa2011@gmail.com
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Intratympanic steroid was suggested by the American Academy Otolaryngology-Head & Neck Surgery SSNHL recommendations, especially following the failure of the first oral therapy.[5]

Unpredictable results of ISSNHL are common with steroid application. Numerous studies have sought to establish a connection between accompanying findings (otoneurological and general examination) and the level of hearing improvement over the past few decades, although with varying degrees of success.[6]

The purpose of the study is to assess variables that could affect the outcome of hearing and to assess the effectiveness of ITS treatment in patients with ISSNHL using discriminant multivariate analysis.

METHODS

Study Design and Patients

For individuals who were diagnosed with ISSNHL between December 2017 and December 2021, a retrospective experimental case series study was undertaken. Cases with known etiology, bilateral SSNHL, uncontrolled diabetes, and patients under the age of 16 were excluded. We only looked into idiopathic cases that sought medical attention within 6 months after onset. The sample size of 186 patients based on an estimate of a clinically relevant advantage of 15 dB in the hearing gain, as a function of power (1 - β error probability) 90%, α error probability at 0.05, and odds ratio (OR) at 0.61 in a 2-tailed z test-logistic regression determined using G*power version 3.1.9.4.

The following information was gathered: age, gender, impaired side, complete blood count, random blood sugar, the interval between when HL first manifested and when therapy began, concurrent symptoms (vestibular and tinnitus), and comorbidities. For each patient, a cranial and temporal bone magnetic resonance imaging (MRI) was done. People who had an inner ear malformation or vestibular schwannoma, lesions that were known to be related to SSNHL on imaging were excluded.

For all patients, pure-tone audiometry (PTA) was used to measure hearing levels at HZ of 500, 1k, 2k, 4k, and 8k. By considering the arithmetic mean of the 500, 1k, 2k, and 4k Hz thresholds, the PTA average was calculated. The audiograms were categorized into upsloping, downsloping, flat, and profound hearing limits at various frequencies.

At 250 and 500 Hz, HL >20 dB was defined as an upsloping curve, whereas a downsloping curve was described as >20 dB diminution between 4k and 8k Hz. It was agreed that an audiometric curve was flat if there were no frequency differences greater than 15 dB.

Using these criteria, the Japan Ministry of Health classified hearing severity into 4 grades: grade 1 (mild), where the mean hearing level was <40 dB; grade 2 (moderate), where the mean PTA level was 40 dB up to 60 dB; grade 3 (severe), where the mean PTA level was >60 dB up to <90 dB; and grade 4 (profound), where the PTA level was >90 dB.[7]

It was documented that the audiometric evaluation was conducted at admission time before treatment and 6 months after it was completed. The hearing gain for each frequency was computed between the pretreatment and posttreatment PTA levels.

At our otology center, 221 patients in total were examined. Eleven patients were excluded because they did not meet the inclusion criteria, whereas 12 patients had an acoustic neuroma detected on an MRI, 6 patients had lost contact, and 2 patients had discounted therapy. The remaining 190 patients gave their permission to participate, and we included them in our study analysis (Figure 1).

Demographics in Figure 2 show the gender and age distribution of cases with ISSNHL (88 males, 102 females); 82 patients were under 40 years and 108 were above 40 years. In the selected cases, 55.8% of patients complained of tinnitus, 22.6% presented with vertigo, and 13.7% with diabetic history. Pure tone audiometery at initial presentation showed the prevalence of moderate grade (42.1%) and descending curve type (52.1%). Totally, 60.5% of patients started treatment protocol less than 1 month.

Therapeutic Protocol

After cleaning of EAC, local anesthesia (cotton soaked with lidocaine spray applied to TM for 10 minutes) was applied. With the head turned to the opposite ear, a 25-gauge needle spinal type was inserted into the anterior–superior portion of the TM for air vent and anticipate bubble arrangement. Next, 0.4-0.6 mL of dexamethasone (8 mg/2 mL) was injected slowly into the posterior–inferior portion of TM (Figure 3) shows steps of IT injections of dexamethasone in a right ear). For at least 30 minutes, the patient was instructed to stay in this posture. Five injections per week were initiated as soon as the diagnosis was made (2 injections were performed in the first week then followed by 1 injection weekly for another 3 weeks.)

As mentioned by Siegel's standards, hearing recovery is defined as a general amplitude of hearing restoration of at least 15 dB, and in cases with bad hearing levels poorer than 75 dB was categorized as no improvement.[8]

Age, gender, the initial level of hearing, the shape of pre-HL PTA curve, pre-HL PTA average, the interval between the beginning of HL and therapy, comorbidities (diabetes), and the existence of tinnitus and vestibular complaints were explored as the predictive variables.

Statistical Analysis

The Statistical Package for Social Sciences version 25.0 (IBM SPSS Corp.; Armonk, NY, USA) was used. One-way analysis of variance was employed to compare numerical variables. Categorical variables were subjected to the Chi-square test. The logistic regression coefficients analyses were used to produce ORs and referring confidence intervals, and significance was defined as a *P* value less than .05. The link between dependent and independent variables was evaluated using discriminant analysis. The dependent variable in discriminant analysis was categorical and nonmetric, and the percentage of correctly classified items serves as an indicator of the discriminant function's effectiveness. The following discriminant linear equation was used to determine the category of the case

$$E = a + B_1 X_1 + B_2 X_2 + B_3 X_3 + \ldots.$$

where E = discriminate function of the dependent variable.

B = discriminant coefficient for independent variable and weight for that variable.

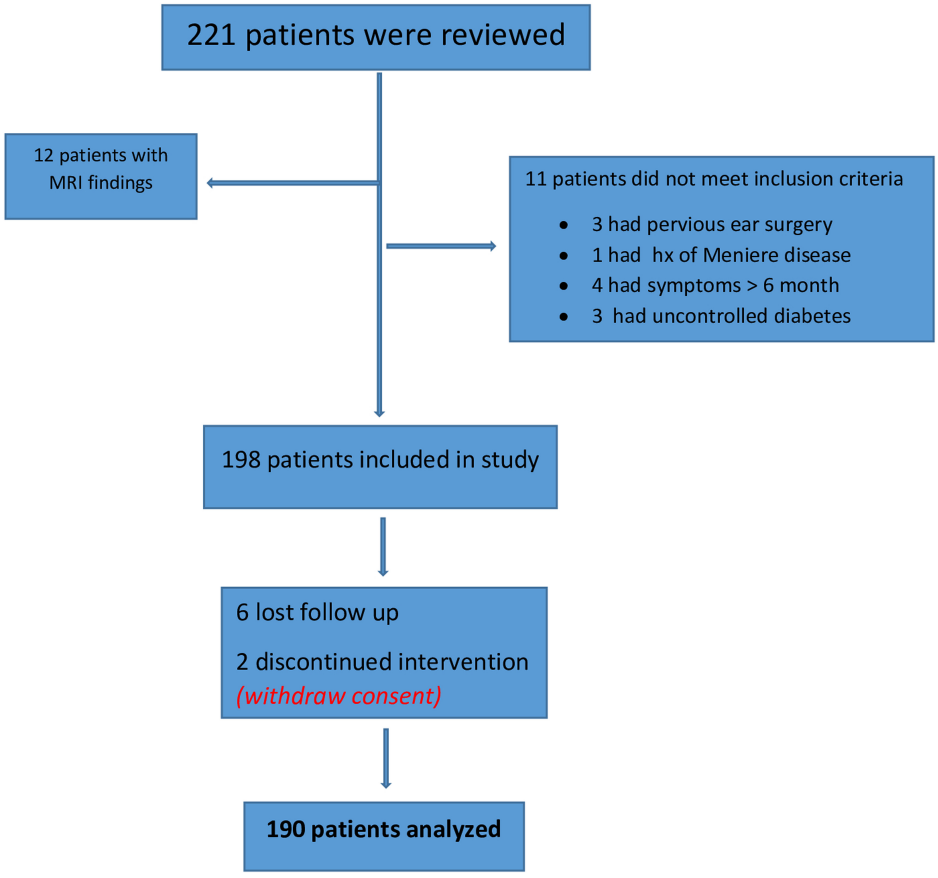

Figure 1. Study flowchart.

X_i = Responses' score for that predictor variable.

a = constant from unstandardized coefficients.

Ethics

All patients were made aware of the procedure's potential hazards, including temporary vertigo, otitis media, and residual TM perforation. They all signed an informed consent form and consented to participate in the study. The Mansoura University-Ethical IRB's Committee approved (Code number: MD/16.08.35) study protocol acceptance.

RESULTS

Clinical outcomes following ITS demonstrate a 72.6% combined recovery rate across all 3 categories (complete in 51 patients, partial in 60 patients, and slight in 27 patients**)** with the remaining patients identified as belonging to the nonrecovery zone.

The relationship between post-ITS injections recovery and demographics is shown in Table 1. Age, tinnitus symptoms, and gender did not statistically affect recovery (*P* value > .05). The highest percentage of non-recovery (30.8%) belongs to profound HL compared to a complete recovery rate of 4.3% (*P* value < .001), moderate degree HL was associated with a high recovery rate (50%) compared to a rate of no recovery (21.2%) (*P* value < .001), the type of audiogram curve had a significant impact on recovery, especially the downsloping type (*P* value < .001), and the absence of vestibular symptoms was observed to effect on recovery.

Diabetic patients were substantially more prevalent in the nonrecovery group, and the hearing recovery group's shorter treatment beginning was significantly greater than that of the nonrecovery group (*P* value <.001).

Univariate analysis in Table 2 states that:

- Parameters (vertigo, diabetes, the onset of treatment, pre-HL PTA type, PTA average, and grade) show a significant result.
- Absence of medical comorbidities, especially diabetics, was positively associated with the hearing recovery group OR of 0.214 (95% CI 0.090-0.505).
- Absence of vertigo was positively associated with recovery group OR was 0.214 (95% CI 0.104-0.441).
- Possibility of hearing recovery had been increased with early IT injections; the weighted mean odds of poor hearing outcomes with delayed treatment for more than 1 month was 3.97 times that with early intervention (95% CI 2.030-7.765).
- The aggregate mean odds of worse results with preinjections grade 4 (profound) hearing grade were .073 times higher than with other grades (95% CI 0.021-0.252). This indicates that the initial audiometric grade was a significant determinant in hearing improvement.

Discriminant analysis was used to determine whether patients with ISSNHL could experience recovery or nonrecovery outcomes using the 9 parameters ordering as shown in Table 1. With Wilks' Lambda = 0.685, Chi-square = 69.407, degrees of freedom = 9, the size of the eigenvalues = 0.460, canonical discriminant functions

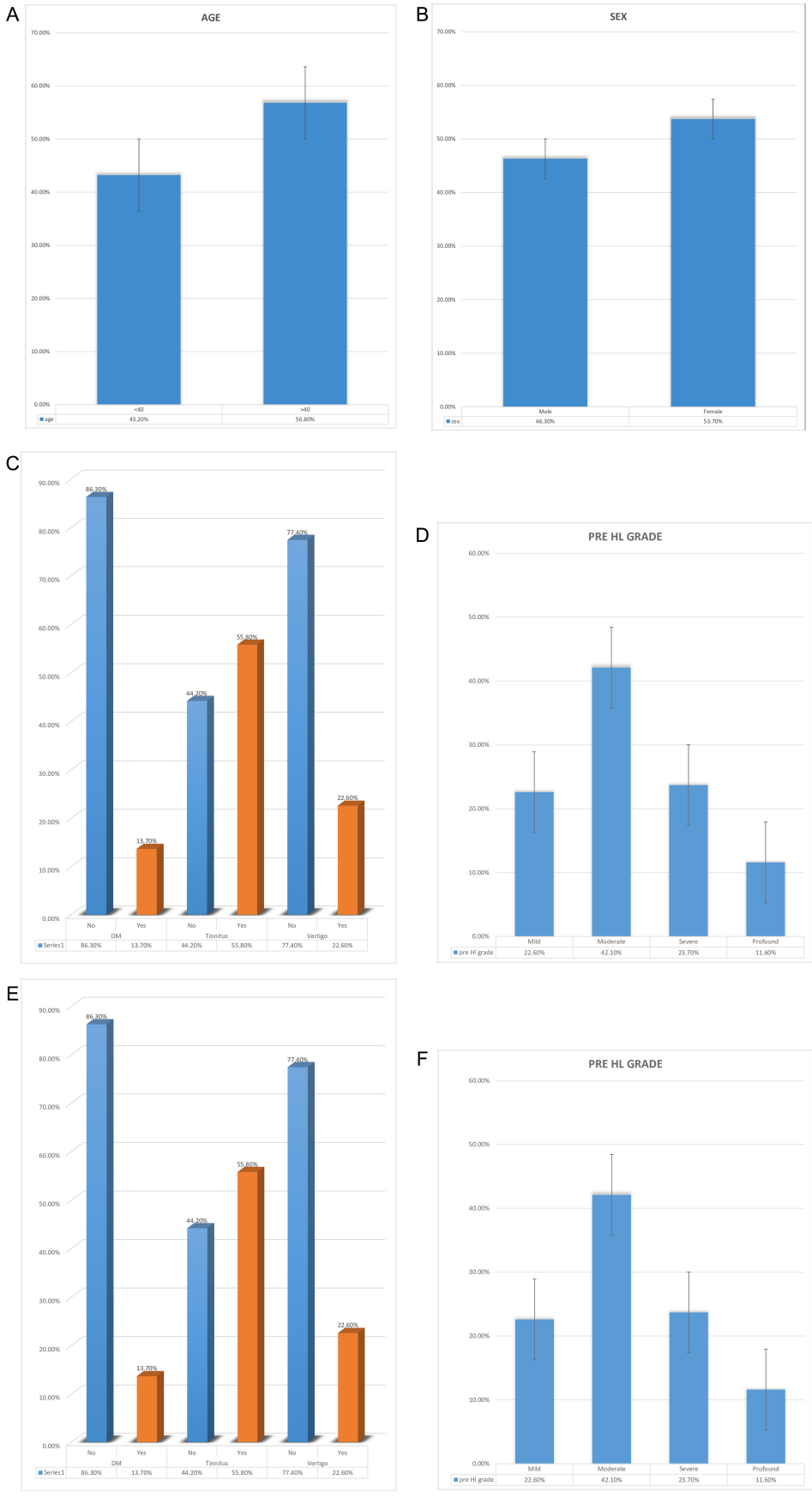

Figure 2. Demographics tables charts. Age (A), gender (B), vertigo, tinnitus, and diabetes (C), pre HL grade (D), PTA type (E), onset period of treatment (F). HL, hearing loss; PTA, pure-tone audiometry.

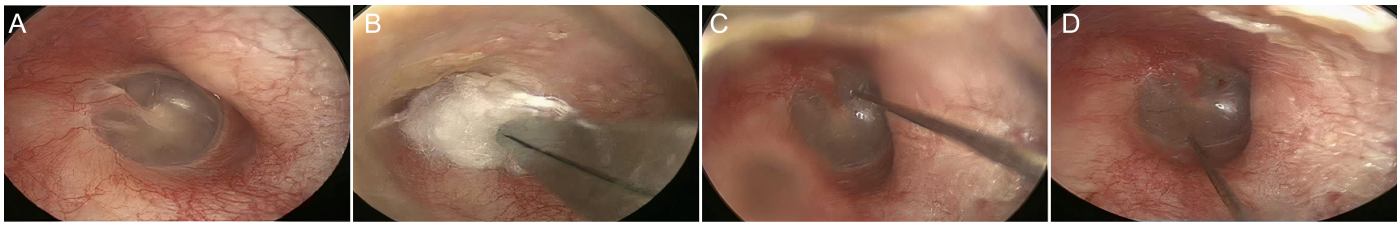

Figure 3. TM examination on the right side (A), local anesthesia to TM using cotton soaked with lidocaine for 20 minutes (B), perforation in the anterosuperior portion of TM to allow air escape (C), ITS in the posteroinferior portion of the TM with a 25-gauge spinal needle (D).

Table 1. Association Between Prognostic Factors and Outcome Measures

Prognostic Factor	Parameter	Ordering	Number		Recovery		No Recovery		*P*
			nm	%	nm	%	nm	%	
Sex	Male	1	88	46.30%	64	46.40%	24	46.20%	.97
	Female	2	102	53.70%	74	53.60%	28	53.80%	
Age	Under 40 y	Real nm	82	43.20%	60	43.50%	22	42.30%	.88
	Above 40 y	Real nm	108	56.80%	78	56.60%	30	57.70%	
Diabetes	Diabetic	1	26	13.70%	11	8.00%	15	28.80%	.001
	Nondiabetic	2	164	86.30%	127	92.00%	37	71.20%	
Peripheral vertigo	Absent	2	147	77.40%	118	85.50%	29	55.80%	.001
	Present	1	43	22.60%	20	14.50%	23	44.20%	
Tinnitus	Absent	2	84	44.20%	64	46.40%	20	38.50%	.32
	Present	1	106	55.80%	74	53.60%	32	61.50%	
Preinjection HL grade	Mild	1	43	22.60%	36	26.10%	7	13.50%	.001
	moderate	2	80	42.10%	69	50.00%	11	21.20%	
	Severe	3	45	23.70%	27	19.60%	18	34.60%	
	Profound	4	22	11.60%	6	4.30%	16	30.80%	
Preinjection PTA type	Flat	1	52	27.40%	45	32.60%	7	13.50%	.001
	Downsloping	2	99	52.10%	75	54.30%	24	46.20%	
	Upsloping	3	17	8.90%	12	8.70%	5	9.60%	
	Profound	4	22	11.60%	6	4.30%	16	30.80%	
Onset time of treatment	Below 1 month	2	115	60.50%	96	30.40%	19	36.50%	.001
	More than 1 month	1	75	39.50%	42	69.60%	33	63.50%	

HL, hearing loss; PTA, pure tone audiometry.

showed a statistically significant difference of .561. Also, 78.9% of the originally grouped instances and 73.7% of the cross-validated grouped cases were properly categorized in the model.

The variables (DM, vertigo, pre-HI average loss, start of medication, and pre-HI grade) in our discriminant model were significant, as shown by the results of the equality tests of group averages. In Table 3, Wilks' lambda demonstrated the measure of a variable's potential and proposed that pre-HI grade, pre-HI average loss, onset 1 month, vertigo, and DM were the best.

The pre-HI grade is the most effective in differentiating between recovery and nonrecovery, according to the structure matrix (Table 3), which depicts the association between each predictor variable and the discriminant function. A positive calculation (pre-HI grade 1, less pre-HI average loss, and onset 1 month) suggested that recovery was likely to be the outcome after ITS Injections, whereas a negative calculation (presence of vertigo, diabetic patients, presence of tinnitus) suggested that ISSNHL nonrecovery was likely to be the outcome after ITS injections and it was unlikely to be needed.

Figure 4 illustrates how the discriminant function was generated using unstandardized canonical discriminant function coefficients for variables that demonstrated substantial intergroup differences (Table 4). Each variable's value or the number 1 or 2 (which corresponds to yes or no in the presence or absence of predictors) was applied to the equation, and a determination was made based on whether the result assumed a positive or negative value. Positive values implied that recovery was likely to occur after ITS Injections.

DISCUSSION

The treatment of ISSNHL is a topic that is still being debated. Although IT corticosteroid treatment when it enters the perilymph through the semipermeable round window is universally acknowledged as the current standard of care, the exact course of the disease is still unknown.

Table 2. Univariate Analysis of Prognostic Factors and Outcome Measures

	Univariate		
	P	OR	95%CI
Age	.885	0.953	0.500-1.817
Gender	.978	0.991	0.523-1.879
Diabetes	<.001*	0.214	0.090-0.505
Tinnitus	.328	0.723	0.377-1.386
Vertigo	<.001*	0.214	0.104-0.441
Prehearing loss grade			
Grade 1 (mild)	<.001		
Grade 2 (moderate)	.705	1.220	0.436-3.416
Grade 3	.016	0.292	0.107-0.797
Grade 4	<.001*	0.073	0.021-0.252
Prehearing loss PTA type			
Flat	<.001		
Downsloping	.124	0.486	0.194-1.219
Upsloping	.141	0.373	0.100-1.387
Profound	<.001*	0.058	0.017-0.200
Onset	<.001*	3.970	2.030-7.765

OR, odds ratio; PTA, pure tone audiometry.

This study will add to the scientific community the discriminant function analysis for clinical outcomes after ITS injection to fire our guns and restore precious hearing in the case of ISSNHL. It is very important to determine which predictive factors we need to focus on for managing ISSNHL. Otologists can predict the clinical outcome results through the discriminant function shown in Figure 4.

The most influential function in good recovery outcomes was pre-HI grade (*F*: 0.616), followed by pre-HI average loss (*F*: 0.525), onset <1 month (*F*: 0.505) absence of vertigo (*F*: 0.493), and absence of diabetes (*F*: 0.415). Gender, age, tinnitus, and pre-HL PTA type did not affect recovery in a statistically meaningful way ($P > .05$).

Table 3. Summary of Canonical Discriminant Function

	Analysis of Case Processing and Test of Equality of Group Means			Structure Matrix*
	Wilks' Lambda	*F*	Significance	Recovery Function
Prehearing loss grade	0.851	32.793	.000	0.616
Prehearing loss average loss	0.887	23.851	.000	0.525
onset < 1 month	0.895	22.023	.000	0.505
Vertigo	0.900	20.981	.000	−0.493
Diabetes	0.927	14.879	.000	−0.415
Tinnitus	0.995	0.954	.330	−0.105
Prehearing loss PTA type	1.000	0.030	.864	0.018
Gender	1.000	0.001	.978	0.003
Age	1.000	0.000	.987	−0.002

PTA, pure tone audiometry.
* Correlations pooled within groups between discriminating variables and standardized canonical discriminant functions

F = 3.091

- **0.014 * age (years)**
- **0.066 * sex (Male/ female) (1 / 2)**
- **0.846 * presence /absence DM (1/2)**
+ **0.128 * presence /absence Tinnitus (1/2)**
- **1.224 * presence /absence Vertigo (1/2)**
+ **1.973 * pre HI average loss (real number)**
- **0.068 * pre HI grade (grade 1 to 4)**
+ **0.057 * pre HL PTA type (flat: 1, downsloping: 2, up: 3, profound: 4)**
+ **0.276 * onset between HL and ITS (real number)**

Figure 4. Discriminant function. *means multiply.

According to our study's results, there is no link between patients aging and improvements in their hearing ($P = .88$) and we agreed with Dispenza et al[9] and Cvorovic et al.[10]

Byl et al.[11] Cinamon et al.[12] Tucci et al.[13] and Moskowitz et al[14] agreed with our study that gender is not a prognostic factor in ISSNHL.

Capaccio et al and Ceylan et al[15,16] come to an agreement with us in accepting vertigo absence as a favorable prognostic factor, and Chung et al[17] and Yu et al[18] showed that the recovery of hearing was not affected by vertigo. Patients with or without tinnitus experienced similar hearing results ($P = .32$).

Patients with or without tinnitus experienced similar hearing results ($P = .32$). This result was consistent with earlier research by Ceylan et al[16], Cvorović et al.[19] and Yu et al.[18] Tinnitus has been noted as a predictive feature associated with higher rates of recovery in studies by Mamak et al[20] and Chung et al.[17]

In our study, early treatment initiation was shown to be a favorable prognostic factor, which was also reported by Hamid et al.[21] Plaza et al.[22] and Kwon et al.[23] However, Kitajiri et al[24] and Bayoumy et al[25] discovered an 81% spontaneous recovery rate in their control group. Particularly on the lower frequencies of SNHL, the spontaneous recovery rate might simulate a beneficial impact of treatment in the early stages of therapy.

Table 4. Unstandardized Canonical Discriminant Function Coefficients

	Function Recovery
Age	−0.014
Gender	−0.066
Diabetes	−0.846
Tinnitus	0.128
Vertigo	−1.224
Prehearing loss average loss	1.973
Prehearing loss grade	−0.068
Prehearing loss PTA type	0.057
Onset less than 1 month	0.276
(Constant)	3.091

PTA, pure tone audiometry.

In Weng et al's[26] research, systemic illness (diabetes mellitus) has been regarded as a poor prognostic indicator in agreement without study, and they were proven to be unrelated to the result in some earlier studies according to Ceylan et al.[16]

Limitations and Drawbacks

This study examined patients with unilateral ISSNHL, with a higher percentage of patients who were nondiabetic and older than 40 years. Retrospective discriminant analysis has only been done after ITS injection; therefore, it is important to compare other therapeutic modalities (systemic steroid and hyperbaric oxygen). Loss of serial follow-up of patients after recovery from ISSNHL may miss additional recurrence. Further research is required for more reliable statistics.

CONCLUSION

Based on the finding of the study, we can state that ISSNHL associated with profound HL, a treatment delay of more than 30 days, the presence of peripheral vertigo, and diabetes were negative prognostic factors. Whereas, age, gender, and presence of tinnitus did not affect prognosis. Patients who have ISSNHL (profound grade 4 and coupled with peripheral vertigo) need to be further investigated. The patient presenting with mild or moderate HL grade and absence of vertigo and controlled glycemic status had a considerably good result, and a more sustained response was observed when ITS injections were introduced during the first 30 days following diagnosis. Through our study, discriminant function equation otologists can estimate the clinical outcome before ITS injection decision.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Mansoura University (Approval No: MD 16.08.35, Date:7-11-2016).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.G., Y.S.; Design – A.A., Y.S.; Supervision – M.G., Y.S.; Resources – M.G., Y.S.; Materials – A.A., Y.S.; Data Processing – A.A., Y.S.; Analysis – Y.S.; Literature Search – A.A.; Writing – A.A.; Critical Review – M.G., Y.S.

Declaration of Interests: The authors have no conflicts of interest to declare.

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