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Predictive factors for recovery in idiopathic sudden sensory neural hearing loss

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Abstract

Background: Idiopathic sudden sensorineural hearing loss (ISSNHL) is considered a clinical symptom of various conditions. Circulatory disorders, viral infection, labyrinthine membrane rupture, and autoimmune reactions are considered as the common causes, but the exact cause remains unestablished. Various drugs and methods have been used empirically for the treatment of ISSNHL. The current study aimed at evaluation factors contributing to the success of standardized medical therapy in cases of ISSNHL.

Methods: In period between 2019 and 2021, a total 40 patients with ISSNHL were enrolled. All patients were subjected to history taking, physical and ENT evaluation. Patients were managed according to the recent guidelines for managing ISSNHL included systemic steroid and salvage therapy.

Results: Mean age of studied patients was 42.55 ± 13.14 years with range between 19 and 70 years. Out of the studied patients; 26 (65%) patients were males and 14 (35%) patients were females. Majority (80%) of patients had no comorbidities. Based on the current study, we found that only 12 (30%) patients were improved while 28 (70%) patients were not improved. It was found that majority (58.3%) of improved patients was females. Frequency of vertigo was significantly higher among patients who were not improved. Three (10.7%) patients of not-improved group and 5 (41.7%) patients of improved group had low lymphocyte:monocytes ratio.

Conclusion: Patients with ISSNHL, the presence of vertigo and late onset of presentation may carry a risk for poor prognosis. Multiple centers studies with large number of patients are warranted to confirm such findings.

Keywords: Sensorineural hearing loss, Lymphocyte:monocytes ratio, vertigo, Systemic steroid

Background

Idiopathic sudden sensorineural hearing loss (ISSNHL) is an otological emergency defined as a hearing loss of more than 30 dB over three consecutive frequencies within 72 h, accompanied by abnormalities of the cochlea, auditory nerve, or central auditory system [1].

The causative etiologies for ISSNHL included viruses, microcirculation abnormalities, and autoimmune disorders. However, definitive evidence remains elusive.

Moreover, non-idiopathic causes of SSNHL must be identified and addressed during the course of management; the most pressing of these are vestibular schwannoma, stroke, malignancy, noise, and ototoxic medications [2, 3].

Much of the literature indicates that 32% to 65% of cases of SSNHL may recover spontaneously. Clinical experience, however, shows that these numbers may be an overestimation. It is important to remember that tinnitus is a frequent comorbidity that may persist and, with time, may become the patient's primary concern [4].

Currently, steroids are the treatment of choice due to their effects on the inner ear such as immunosuppression and circular enhancement. Combined systemic and

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intra-tympanic steroid treatment has previously been reported to be beneficial for SSNHL patients, with overall better treatment outcomes [5, 6].

This work was designed to evaluate the factors contributing to the success or failure of standardized medical therapy in cases of ISSNHL. Also, to detect the degree of correlation of the presenting symptoms and comorbidities to the patient final hearing prognosis.

Methods

Study setting and design

A cross-sectional observation study was conducted at outpatients clinics of ENT Department in period between 2019 and 2021.

Selection criteria

Inclusion criteria

All cases above 6 years presented with unilateral or bilateral ISSNHL were enrolled.

Exclusion criteria

Exclusion criteria include congenital causes such as dilated vestibular aqueduct, post-traumatic sudden sensory hearing loss, labyrinthitis caused by otitis media, perilymph fistula, neoplasia and/or cerebrovascular accidents.

Methodology

Full history taking was done including age sex side of hearing loss residence, occupation, duration of clinical symptoms and associated symptoms. History of similar condition, trauma, ototoxic drugs, and family history were recorded. Comorbidities as hypertension, diabetes mellitus, and neurological disease were also, recorded.

Thorough general and local evaluation was done. Full ENT examination included inspection, auricle (deformity, swelling, scar, tenderness), external auditory canal, tympanic membrane, middle ear (pale, dry, congested mucosa). Other examinations were done as fistula sign, tuning fork test, Rinne and Weber tests. In addition to facial nerve evaluation.

The following laboratory data were ordered: complete blood count, lymphocyte:monocyte ratio, renal function, liver function tests, and random blood sugar.

Pure tone audiometry was performed in a sound proof booth by an audiologist at 0.5, 1, 2, 3, 4, and 6 kHz in both ears via an automated diagnostic audiometer (SA 203, Entomed, Sweden). The mean threshold values of both ears were used. Low-frequency hearing was defined as average thresholds of 0.5, 1, and 2 kHz. High-frequency hearing was defined as average thresholds of 3, 4, and 6 kHz. degree of SNHL (mild, moderate, severe, profound, or total,) and speech discrimination (poor, fair, good, excellent).

MRI brain with gadolinium to exclude vestibular schwannomas.

Management plans

The patients were managed according to the recent guidelines for managing ISSNHL as follows [7]:

- A) All patients with ISSNHL presented early (in the first 2 weeks) received systemic steroid prednisolone (1–2 mg/kg/day) according to the body weight in two divided doses for 7 days, followed by 5 days tapering
- B) Salvage treatment:

1. Patients were managed by 4 sessions of intratympanic steroid after failure of systemic steroid, each session was 4 days apart. The injection was done under local anesthesia and microscope magnification. Patient in supine position while the patient tilted the head 45° to the healthy side. After the surgeon confirmed intact tympanic membrane and middle ear status, a pack of lignocaine gel conc 2% was applied in the floor of the external canal for 10 min to induce anesthesia by using insulin syringe bore.

After removal of anesthetic agent and sterilization of the external canal with 70% ethanol, an 0.8 ml of hydrocortisone was injected in the middle ear through postero-inferior part of tympanic membrane to reach the round window to the cochlea. The patient was instructed to avoid swallowing or moving for 30 min remaining in the same position.

2. If the patient come late (after 2 weeks), patients were managed by 4 sessions of intratympanic steroid injection from the start, each session was 4 days apart.
3. If systemic corticosteroids were contraindicated (hypertensive, diabetic patient, closed angle glaucoma patient), patients were managed by 4 sessions of intratympanic steroid injection from the start, each session was 4 days apart

- C) All the patients received antiviral medication in the form of acyclovir and valacyclovir. Also, they received vasodilator.

Follow-up

All the patients were subjected to audiological evaluation using audiogram 2 weeks and 4 weeks after initiation of therapy to detect the treatment outcome.

Statistical analysis

Data was collected and analyzed by using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, NY). Quantitative data were expressed as mean ± standard deviation (SD) and compared with Student's *t* test. Nominal data were given as number (*n*) and percentage (%). Chi² test was implemented on such data. Level of confidence was kept at 95% and hence, *P* value was considered significant if < 0.05.

Results

Baseline data of studied patients (Table 1)

Mean age of studied patients was 42.55 ± 13.14 years with range between 19 and 70 years. Out of the studied patients, 26 (65%) patients were males and 14 (35%) patients were females.

As regards onset of hearing loss, it was noticed that 14 (35%) and 26 (65%) patients had onset of loss less and more than 2 weeks, respectively. Majority (82.5%) of patients had unilateral hearing loss and only 7 (17.5%) patients had bilateral hearing loss. Four (10%), 3 (7.5%), and 1 (2.5%) patients had diabetes mellitus, hypertension, and chronic kidney diseases, respectively.

Mild, moderate, severe, profound, and total hearing loss were present in 2 (5%), 15 (37.5%), 12 (30%), 2 (5%), and 9 (22.5%) patients, respectively. Nine patients (22.5%) patients had high frequency while only two (5%) patients had low frequency.

Eight (20%) patients had zero speech discrimination while 11 (27.5%) and 21 (52.5%) patients had poor and good speech discrimination, respectively. Only 8 (20%) patients had low lymphocyte:monocytes ratio while 32 (80%) patients had normal lymphocyte:monocytes ratio.

Therapy and outcome among studied patients (Table 2, Fig. 1)

Majority (65%) of patients received intratympanic steroid and only 5 (12.5%) patients received systemic steroid. There were 9 (22.2%) patients received intratympanic with steroid. Only 12 (30%) patients were improved while 28 (70%) patients were not improved.

Therapy and outcome among studied patients (Table 2, Fig. 1)

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Table 1 Baseline data of studied patients

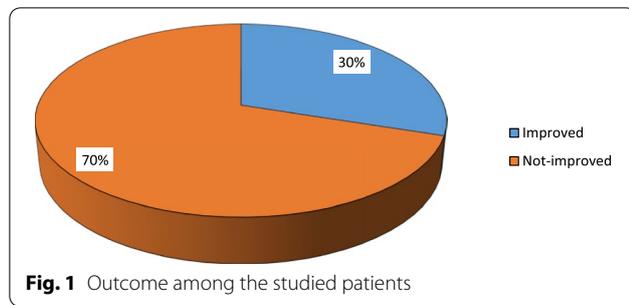
	N = 40
Age (years)	42.55 ± 13.14
Range	19–70
Sex	
Male	26 (65%)
Female	14 (35%)
Comorbidities	
None	32 (80%)
Diabetes mellitus	4 (10%)
Hypertension	3 (7.5%)
Chronic kidney disease	1 (2.5%)
Onset of hearing loss	
Less than 2 weeks	14 (35%)
More than 2 weeks	26 (65%)
Hearing loss	40 (100%)
Laterality	
Unilateral	33 (82.5%)
Bilateral	7 (17.5%)
Tinnitus	37 (92.5%)
Vertigo	20 (50%)
Degree of hearing loss	
Mild	2 (5%)
Moderate	15 (37.5%)
Severe	12 (30%)
Profound	2 (5%)
Total	9 (22.5%)
Frequency	
All	29 (72.5%)
High	9 (22.5%)
Low	2 (5%)
Speech discrimination	
Zero	8 (20%)
Poor	11 (27.5%)
Good	21 (52.5%)
Lymphocyte:monocyte ratio	
Low	8 (20%)
Normal	32 (80%)

Data expressed as frequency (percentage), mean (SD), range

Table 2 Therapy and outcome among studied patients

	N = 40
Therapy	
Systemic steroid	5 (12.5%)
Intratympanic steroid	26 (65%)
Intratympanic with systemic steroid	9 (22.5%)
Outcome	
Improved	12 (30%)
Not-improved	28 (70%)

Data expressed as frequency (percentage)



Characteristics of patients based on the outcome (Table 3, Figs. 2, 3, 4, and 5)

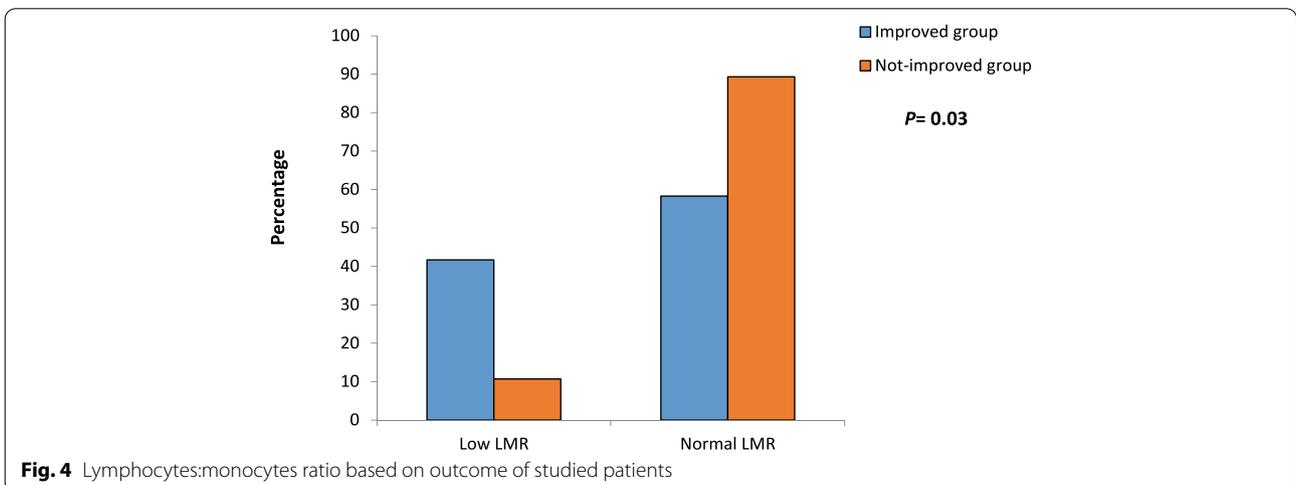
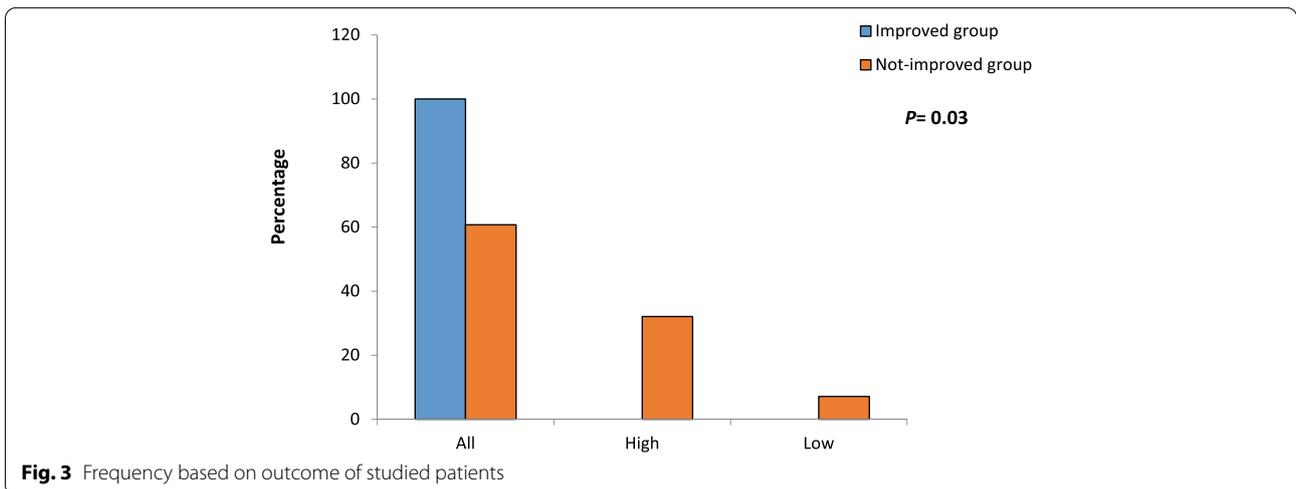
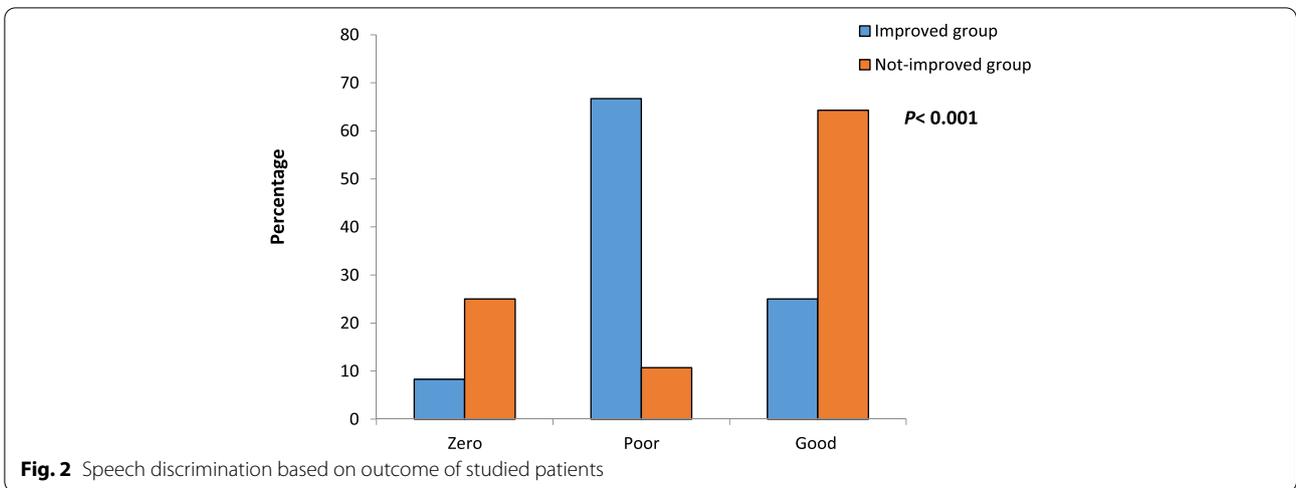
It was found that majority (58.3%) of improved patients was females while majority (75%) of not-improved group was males with significant difference between both groups ($p = 0.04$). Frequency of vertigo was significantly higher among patients who were not improved (17 (60.7%) vs. 3 (25%); $p = 0.03$).

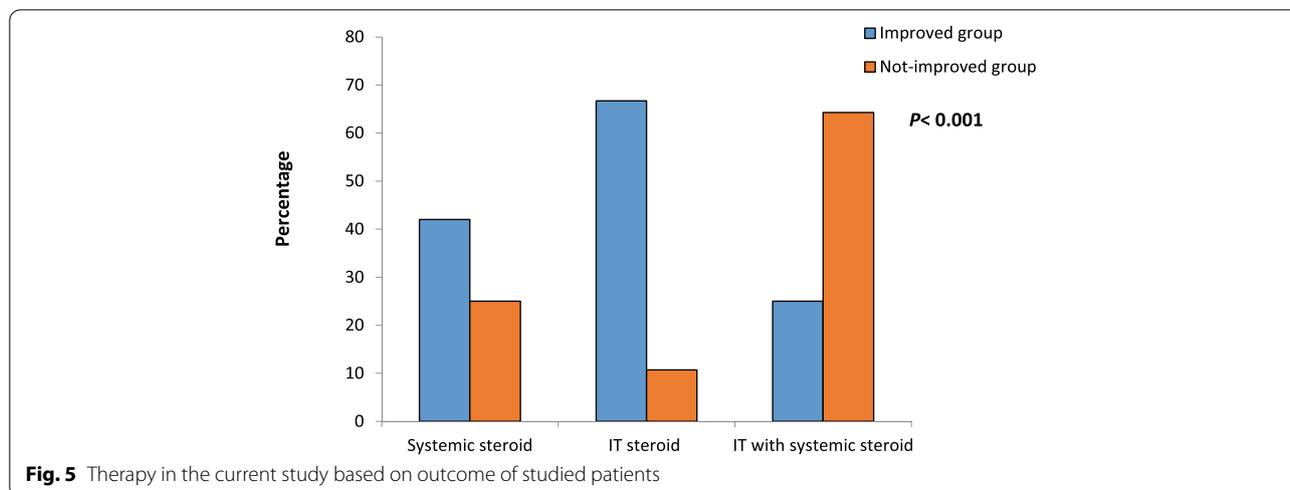
Majority (66.7%) of improved patients had poor discrimination while majority (64.3%) of not-improved group had good discrimination with significant difference between both groups ($p < 0.001$). Also, all improved patients had all frequency while 17 (60.7%), 9 (32.1%),

Table 3 Characteristics of patients based on the outcome

	Improved (n = 12)	Not-improved (n = 28)	P value
Age (years)	38.83 ± 14.40	44.14 ± 12.49	0.24
Sex			0.04
Male	5 (41.7%)	21 (75%)	
Female	7 (58.3%)	7 (25%)	
Onset of hearing loss			0.04
Less than 2 weeks	7 (58.3%)	7 (25%)	
More than 2 weeks	5 (41.7%)	21 (75%)	
Laterality			0.06
Unilateral	12 (100%)	21 (75%)	
Bilateral	0	7 (25%)	
Tinnitus	11 (91.7%)	26 (92.9%)	0.66
Vertigo	3 (25%)	17 (60.7%)	0.04
Degree of hearing loss			0.08
Mild	0	2 (7.1%)	
Moderate	2 (16.7%)	13 (46.4%)	
Severe	2 (16.7%)	0	
Profound	5 (41.7%)	7 (25%)	
Total	3 (25%)	6 (21.4%)	
Frequency			0.03
All	12 (100%)	17 (60.7%)	
High	0	9 (32.1%)	
Low	0	2 (7.1%)	
Speech discrimination			< 0.001
Zero	1 (8.3%)	7 (25%)	
Poor	8 (66.7%)	3 (10.7%)	
Good	3 (25%)	18 (64.3%)	
LMR			0.03
Low	5 (41.7%)	3 (10.7%)	
Normal	7 (58.3%)	25 (89.3%)	
Comorbidities	2 (16.7%)	6 (21.4%)	0.54
Therapy			< 0.001
Systemic steroid	5 (41.7%)	0	
IT steroid	5 (41.7%)	21 (75%)	
IT with systemic steroid	2 (16.7%)	7 (25%)	

Data expressed as frequency (percentage), mean (SD). P value was significant if < 0.05 CKD chronic kidney disease, LMR lymphocyte:monocyte ratio, IT intratympanic





and 2 (7.1%) patients of non-improved group had all, high, and low frequency, respectively.

Only 3 (10.7%) patients of not-improved group and 5 (41.7%) patients of improved group had low lymphocyte:monocytes ratio with significant difference between both group ($p = 0.03$). The majority (58.3%) of improved patients had onset was less than 2 weeks while majority (75%) of not-improved group had onset more than 2 weeks with significant difference between both groups ($p = 0.04$).

None of not-improved group received systemic steroid alone while 7 (25%) patients of them received IT while systemic steroid while 21 (75%) of them received IT steroid alone. In case of improved group; 5 (41.7%) patients received systemic steroid alone and another 5 (41.7%) patients received IT steroid alone and only two patients received IT with systemic steroid with significant differences between both groups (< 0.001).

Discussion

An important element of research on ISSHL is to identify prognostic factors for this disease. Many studies have described predictive indicators to identify patients with a good prognosis needing no or minimal treatment. Some of these studies have concluded that the earlier the patient receives treatment, the better the outcome

The most widely accepted treatment options for ISS-NHL are systemic steroid therapy and ITS injection. Nonetheless, it is important treatment be started immediately, because time is limited and treatment initiated after 30 days is unhelpful because damage at this time is permanent. Systemic steroids are the major agents used due to their potent anti-inflammatory effects

Based on this study, it was found that only 12 (30%) patients were improved while 28 (70%) patients did

not improve. This low frequency of recovery could be explained by majority (65%) of patients came with late onset that exceeded 2 weeks. The majority of studies on adult ISSNHL patients have concluded presentation at > 10 days after hearing loss results in poor outcomes [8–11].

Another explanation for this point in the current is that severity of hearing loss ranged between severe to total hearing loss in majority of patients (23 patients; 57.5%). It is known that patients with a down-sloping hearing pattern or profound hearing loss showed a tendency toward poor hearing recovery [12].

In comparison between patients who achieved improved hearing loss and those did not achieve improvement, we found that both groups had insignificant difference as regards age and comorbidities but majority (58.3%) of improved patients was females while majority (75%) of not-improved group was males. Also, frequency of vertigo was significantly higher among patients without improvement (17 (60.7%) vs. 3 (25%); $p = 0.03$).

This was in line with Uhm et al. (2021) who found that both recovery and non-recovery groups had insignificant difference as regards age and comorbidities among studied patients. They also, reported that recovery rate was higher among females' patients in comparison to males' patients but with no significant effect in regression analysis (72.6% vs. 63.3%) [13].

Shimanuki et al. (2021) although they found that sex had no statistical effect on the recovery of ISSNHL but they noticed that patients who did not achieve improvement had significant higher mean age (62 vs 56 years; $p < 0.001$). Also, they agreed with our results and found higher frequency of vertigo among patients without improvement (33.6% vs. 11.9%; $p < 0.001$) [14].

In another study, baseline characteristics included age, sex, comorbidities, and frequency of vertigo had no significant differences between improved and not-improved patients [11]. These differences in the reported studies as regards effect of patients' characteristics' on outcome of ISSNHL may be attributed to different sample size, selection criteria, and duration and type of therapy

We found that tinnitus was frequently found in all patients either recovery or non-recovery group. In some previous reports, tinnitus was found to be a positive prognostic factor and dizziness to be a negative prognostic factor of adult ISSNHL outcome. Ha et al. (2019) found that 33.3% of their patient cohort had accompanying dizziness and 78.6% had tinnitus. They found significant positive relation between tinnitus recovery but no relation between dizziness and recovery [11].

In the current study, regarding onset of symptoms, it was found that majority (58.3%) of improved patients had onset was less than 2 weeks while majority (75%) of not-improved group had onset more than 2 weeks with significant difference between both groups ($p = 0.04$). this was consistent with many previous studies that concluded treatment should be started immediately, because time is limited and treatment initiated after 30 days is unhelpful [12, 13, 15, 16].

Considering the treatment prognoses of 494 patients with ISSHL, Kang et al. (2017) identified age, histories of diabetes and dyslipidemia, co-presentation of dizziness, duration between symptom onset and treatment, initial PTA results, speech discrimination score, treatment methods, and duration between symptom onset and ITSI administration as prognostic factors [17].

In the current study, we found that improved patients had higher frequency of low LMR (41.7% vs. 10.7%; $p = 0.03$) in comparison to those failed to recover. There are several measures of inflammatory status have been proved to be significantly associated with ISSHL in clinical practice, including white blood cell count, interleukin 6 (IL-6), C-reactive protein, tumor necrosis factor- α , neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) [18].

Recently, Gupta et al. (2021) showed no significant difference seen in the group with and without improvement concerning gender, duration, and other laboratory investigations and NLR and LMR ratio [19].

Ha et al. (2019) observed NLR and PLR values were significantly higher in the ISSNHL group than in normal controls. Also, we found that NLR and PLR values increased as the hearing recovery was poor in ISSNHL patients. But, in comparisons of each group of ISSNHL patients and control group, it was difficult to conclude that PLR value has any statistically significant meaning [11].

The main limitations of the current study included: (1) relatively small sample size, (2) short-term follow-up of those patients and (3) the study performed in only one center. We plan to increase the number of cases and examine the prognostic predictors according to the severity of hearing loss in future studies with multiple centers studies.

In conclusion, poor initial hearing level, presence of vertigo, and late onset of presentation were identified as poor predictors of hearing recovery after ISSHL. In patients with these pre-treatment factors, hearing recovery is unlikely and early additional treatment may be considered. Also, it is recommended to perform such studies with increase the number of cases and examine the prognostic predictors according to the severity of hearing loss in future studies with multiple centers studies.

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Authors' contributions

MA have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. SA have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data and have been involved in drafting the manuscript or revising it critically for important intellectual content. MA have given final approval of the version to be published. ES have given final approval of the version to be published. MO agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Review Board of Faculty of Medicine, Assiut University. Informed written consent was obtained from all participants according to the Declaration of Helsinki. This study was registered on clinicaltrials.com with NCT 05112354.

Consent for publication

Verbal consent was taken from participants for publication.

Competing interests

The authors declare that they have no competing interests.

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