

RESEARCH ARTICLE

Evaluation of Systemic Immune-Inflammation Index in Patients With Idiopathic Sudden Sensorineural Hearing Loss

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Abstract

Introduction: Systemic immune-inflammation index (SII) is an indicator of the inflammatory process. In this study we aimed to determine whether there is a relationship between the level of hearing loss and SII in patients diagnosed with idiopathic sudden sensorineural hearing loss (ISSHL), and to reveal whether SII has an indicator in the rate of improvement in hearing loss after treatment. **Methods:** Patients with ISSHL were included in the study. According to the audiometry performed before the initial treatment, the patients were divided into 3 groups (250, 500, 1000, 2000, 4000, 8000 Hz pure tone averages) below 40 dB defined as mild, between 40 and 80 dB defined as moderate and above 80 dB defined as severe. **Results:** In total 201 patients, 64 were in the mild hearing loss group, 115 in the moderate hearing loss group, and 22 in the severe hearing loss group. Multivariable logistic regression analysis revealed that higher SII [OR=1.002, 95% CI(1.001-1.003); p<0.001] associated with the severity of hearing loss. A statistically significant difference was found between the mean SII of the three groups (p<0.001). A negative correlation was found between improvement in hearing loss after treatment and SII levels. (R=-0.195, p<0.001). In addition, a negative correlation was found between the improvement in hearing loss and SII (R=-0.195, p<0.001). **Conclusion:** SII is an easily available and relatively cheap marker, was associated with the severity of hearing loss. In addition, it was also associated with the recovery of hearing loss.

Article Info

Received Date: 27.03.2023

Accepted Date: 01.04.2023

Keywords:

Idiopathic sudden sensorineural hearing loss, systemic immune-inflammation index, prognosis, marker

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Introduction

Idiopathic sudden sensorineural hearing loss (ISSHL) is a sensorineural hearing loss of 30 dB and above, which develops in three days or less and is seen in three consecutive frequencies in audiometry.¹ This disease, which is an otolaryngology emergency, is usually seen unilaterally. While viral infections are the most common etiology for sudden sensorineural hearing loss, vascular pathologies, autoimmune diseases, inflammatory conditions, acoustic neuroma may also be the underlying cause.² Sudden sensorineural hearing loss is not idiopathic; when a cause is found in the etiology. Although the etiology is not fully known, the association of ISSHL with chronic inflammation and the relationship between inflammatory markers and cochlear damage have been proven in previous studies.³⁻⁴ Since the cochlea is fed by a single terminal branch, diseases such as thrombotic events, hypertension and diabetes mellitus that may cause impaired perfusion may predispose to the formation of ISSHL.⁵

Systemic immune-inflammation index (SII) is an inflammatory biomarker calculated by peripheral neutrophil, lymphocyte and platelet count (Neutrophil x Platelet count/Lymphocyte count).⁶ It has been shown that high SII are associated with lower survival, recurrence of malignancies, and decreased response to treatment in malignancies.⁷⁻⁸ Additionally, there are studies showing that higher SII, which is thought to be an indicator of increased inflammation, associated with adverse cardiovascular outcomes.⁹⁻¹¹

Even if it is known that a higher inflammation is associated with the severe hearing loss,³ to date, there is only one study that shows SII is higher in patients with ISSHL compared with control group.¹² However the role of SII in the severity of ISSHL patients is unknown. Therefore, in the current study, we aimed to determine whether there is a relationship between the level of hearing loss and SII in patients diagnosed with ISSHL, and to reveal whether SII has an indicator in the rate of improvement in hearing loss after treatment and SII values.

Material and Methods

This study was carried out by retrospectively examining the electronic health records of patients who were diagnosed with sudden hearing

loss in the otorhinolaryngology clinic between the dates of 20 Feb, 2019 and 1 Dec, 2021 in our hospital. Ethics approval was obtained from the institutional review board prior to initiation of the study (No.2 clinical research ethics committee).

Patients with a sensorineural hearing loss of 30 dB or more, which developed suddenly in the last three days, seen at 3 consecutive frequencies, were included in the study.

Patients with otological disease, malignancy, active infectious disease were excluded from the study. Complete blood count, liver function tests, kidney function tests, thyroid function tests, lipid profile, albumin, sedimentation and viral serology tests were studied from the patients included in the study before starting the treatment. SII was calculated for each patient using the Neutrophil x Platelet/Lymphocyte formula for complete blood count.⁶

According to the audiometry performed before the initial treatment, the patients were divided into 3 groups (250, 500, 1000, 2000, 4000, 8000 Hz pure tone averages) below 40 dB defined as mild, between 40 and 80 dB defined as moderate and above 80 dB defined as severe.¹³ As a standard treatment protocol, intravenous methylprednisolone treatment of 1 mg/kg per day was given to all patients for the first 3 days, and the dose was gradually reduced 10 mg every 2 days.

Age, gender, complete blood counts, SII values, pure tone averages in the first audiometry, pure tone averages in the audiometry performed 1 month after the treatment, and the difference between the first audiometry pure tone averages and the pure tone averages in the last audiometry of all patients were recorded.

Statistical analysis

Categorical variables were presented in frequency tables. Continuous variables were presented (mean, standard deviation (SD), or median, and interquartile ranges between 25% and 75%, as appropriate. Binary comparisons of numerical variables not conforming to a normal distribution were carried out using the Mann-Whitney U test. Correlation between age, gender and blood parameters according to mild, moderate and severe hearing loss groups in the first audiometry were presented. Univariable logistic regression analyses were performed to

investigate the predictors of ISSHL. Consequently, a multivariable logistic regression analysis (variables selected from univariable logistic regression analyses with a p-value less than 0.10) was performed to investigate significant independent predictors of ISSHL.

The correlation between the SII values and first audiometry values was plotted. The correlation between the SII values and the difference in the first audiometry and 1-month follow-up audiometry was also plotted. Correlations between the SII and hearing loss values were examined using the Pearson correlation analyses.

The receiver operating characteristic (ROC) curve was used to evaluate the performance of SII to predict hearing loss (first audiometry) and hearing loss recovery (the difference in the first audiometry and 1-month follow-up audiometry). All statistical analyses were performed in Stata version 17.0 (Stata Corporation, College Station, TX, USA). Statistical significance was defined as a p-value of less than 0.05.

Result

A total of 201 (99 male, 102 female) patients with sudden hearing loss were included in the final analyses. The mean and standard deviation (SD) age of patients 43.9 (14.4). When the patients are grouped as mild, moderate and severe hearing loss; there was no statistically significant difference between the three groups in terms of gender ($p=0.875$), hemoglobin levels ($p=0.59$), neutrophil

counts ($p=0.11$), platelet counts ($p=0.84$), albumin ($p=0.36$), and lymphocyte counts ($p=0.16$). A statistically significant difference was found between the three groups in terms of age ($p=0.046$), white blood cell counts ($p=0.026$), monocyte counts ($p=0.017$), and SII values ($p<0.001$). All demographic information and laboratory results of the patients are presented in Table 1.

Multivariable logistic regression analysis revealed that higher age [odds ratio (OR)=1.039 confidence intervals (95% CI) 1.011-1.067; $p=0.005$], higher monocyte count [OR=26.368, 95% CI (1.304-533.095); $p=0.033$] and higher SII [OR=1.002, 95% CI (1.001-1.003); $p<0.001$] associated with the severity of hearing loss (Table 2). As shown in Figure 1, there was a significant positive correlation between the level of hearing loss and SII ($R=0.461$, $p<0.001$). The discrimination of the SII to predict hearing loss as assessed by ROC curve was 0.864 (Figure 2). As shown in Figure 3, the difference between the pure tone averages in the audiometry performed before the start of the treatment and the pure tone averages in the audiometry performed 1 month later was examined, a negative correlation was found between the improvement in hearing loss and SII ($R=-0.195$, $p<0.001$). The discrimination of the SII to predict hearing loss recovery as assessed by ROC curve was 0.663 (Figure 4).

Table 1: Demographic information and laboratory results of the patients

	Total N=201	Mild N=64	Moderate N=115	Severe N=22	p-value
Age	43.90 (14.44)	40.22 (11.49)	45.54 (15.53)	46.05 (14.82)	0.046*
Male	99 (%49.3)	31 (%48.43)	57 (%49.57)	11 (%50.0)	0.875
WBC (x109/L)	8.23 (2.75)	7.50 (2.06)	8.74 (3.09)	7.97 (2.42)	0.026*
Platelets (x109/L)	257.17 (60.60)	256.12 (60.61)	256.11 (60.00)	264.23 (65.35)	0.84
Neutrophils (x109/L)	5.31 (2.62)	4.74 (2.15)	5.67 (2.91)	5.25 (2.24)	0.11
Lymphocytes (x109/L)	2.13 (0.71)	2.06 (0.67)	2.22 (0.74)	1.94 (0.65)	0.16
Monocytes (x109/L)	0.44 (0.17)	0.39 (0.11)	0.47 (0.19)	0.47 (0.19)	0.017*
HGB (g/dL)	14.50 (1.54)	14.33 (1.54)	14.58 (1.56)	14.60 (1.51)	0.59
ALT (U/L)	26.25 (14.62)	24.16 (11.30)	27.29 (14.64)	27.10 (21.15)	0.44
AST (U/L)	21.25 (8.86)	21.85 (10.07)	21.01 (8.74)	20.71 (5.70)	0.82
TSH (mU/L)	2.12 (2.02)	2.20 (2.07)	2.16 (2.13)	1.81 (1.50)	0.81
SII	737.83 (477.59)	543.16 (315.32)	718.05 (417.77)	1315.21 (603.57)	<0.001*

The values are presented as mean (SD)

Abbreviations: WBC: White Blood Cell, HGB: Hemoglobin, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, TSH: Thyroid Stimulating Hormone, SII: Systemic Immune-Inflammation Index

Discussion

The underlying cause of ISSHL is not clearly known. Although its etiopathogenesis is controversial, infectious, inflammatory, immunological causes and microvascular pathologies are frequently seen as etiological factors.³ The fact that hearing loss does not always benefit from treatment or that it partially improves has been effective in investigating the factors affecting the prognosis of the disease. Prior studies, showed that severe hearing loss, the long period between the onset of hearing loss and the treatment given, hearing loss is accompanied by vertigo, hearing loss at high frequencies, the patient has hypertension, diabetes mellitus, hyperlipidemia, vascular diseases, and advanced age are negative prognostic factors.¹⁴⁻¹⁷ Young age and accompanying tinnitus were found to be positive prognostic factors.¹⁸

In recent years, various inflammation markers related to the severity, prognosis and response to treatment of ISSHL, and calculations of blood values related to the inflammation process such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) have attracted the attention of researchers.¹²⁻¹⁹⁻²⁰ We also think that clues that can give an idea about the disease process and treatment response can guide the treatment management of the disease. For example, in patients who are predicted to have a poor

prognosis, approaches such as adding hyperbaric oxygen therapy to steroid therapy can be decided in advance. In their study, Li et al. found that the decrease in NLR rates after hyperbaric oxygen therapy in ISSHL patients was associated with hearing gains.²¹

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SII was first used by Hu et al. to determine the prognosis in patients undergoing curative resection of hepatocellular cancer, and high SII values were found to be associated with poor prognosis.⁶ It has been used in many studies on malignancy patients in the following years, and it has been found to be a more powerful tool than NLR and PLR in determining the prognosis in colorectal cancer and cervical cancer.²²⁻²³ SII has been studied in malignancies in the otolaryngology field, and it has been found to be an important value in predicting prognosis in nasopharyngeal cancers,²⁴ it was found to be higher in patients with laryngeal cancer compared to the control group, and it was reported that it can give important clues for perineural invasion and lymphatic spread.²⁵

There is only one study investigating SII values in ISSHL.¹² In that study, Ulu et al. showed that SII may be a diagnostic marker in ISSHL, it was determined that patients with high SII values may not have a treatment response, and it was reported that larger studies are needed to understand the importance of SII in ISSHL.¹² In the study of İkinçioğulları et al., NLR and PLR values were found to be higher in ISSHL than in the control group, and it was found that patients with higher NLR values had a better response to treatment.²⁶ On the other hand, in the study of Aydoğdu et al., NLR values were found to be higher in the group with no improvement in hearing loss than in the group with improvement.²⁷ In our study, we investigated the relationship between the level of hearing loss and SII values and found that SII values were higher as hearing loss increased. When we looked at the treatment response, we found that the response to treatment was worse in patients with high SII values.

Since inflammatory events are the underlying cause of ISSHL etiology, inflammatory markers can provide important information about the severity, prognosis and response to treatment of the disease. For this reason, markers that give an idea about the inflammatory process have always attracted the attention of researchers. While researching new markers, the correlation with the severity and prognosis of the disease, being easily accessible, practical and inexpensive are important criteria. This study has several limitations that must be taken into account when evaluating the findings. First, the comorbidities of the patients,

Table 2: Factors associated with the severity of hearing loss

Multi Variable Logistic regression

	Odds Ratio	95% Confidence intervals	p-value
Age	1.039	1.011-1.067	0.005
WBC (x109/L)	1.021	0.853-1.222	0.823
Monocytes (x109/L)26.368		1.304-533.095	0.033
SII	1.002	1.001-1.003	0.002

Abbreviations: WBC: White Blood Cell, SII: Systemic Immune-Inflammation Index

prognosis, approaches such as adding hyperbaric oxygen therapy to steroid therapy can be decided in advance. In their study, Li et al. found that the decrease in NLR rates after hyperbaric oxygen therapy in ISSHL patients was associated with hearing gains.²¹

SII was first used by Hu et al. to determine the prognosis in patients undergoing cura-

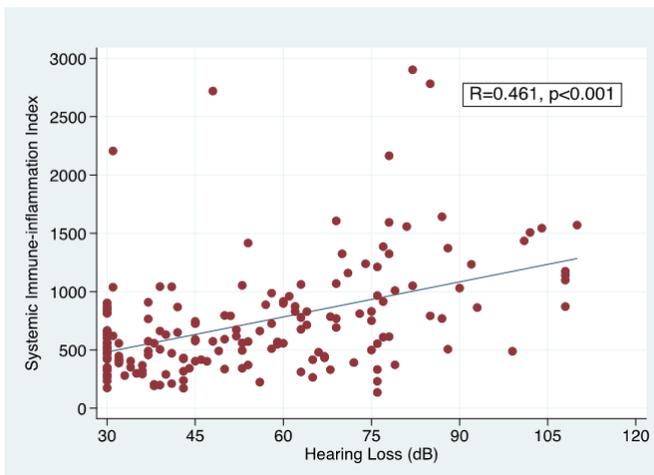


Figure 1: Correlation between the level of hearing loss and systemic immune-inflammation index

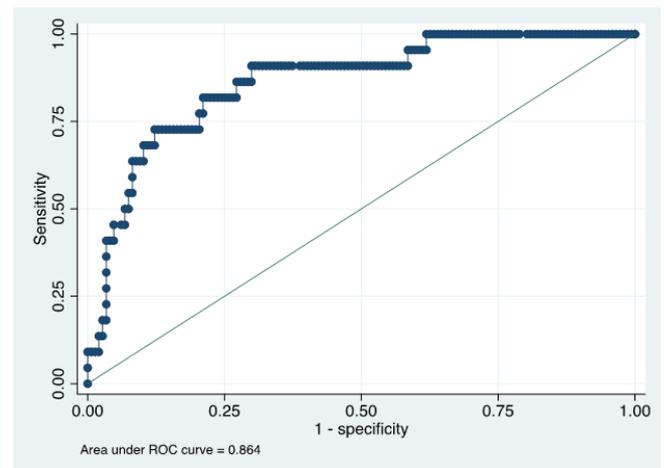


Figure 2: Receiver operating characteristic curves of hearing loss

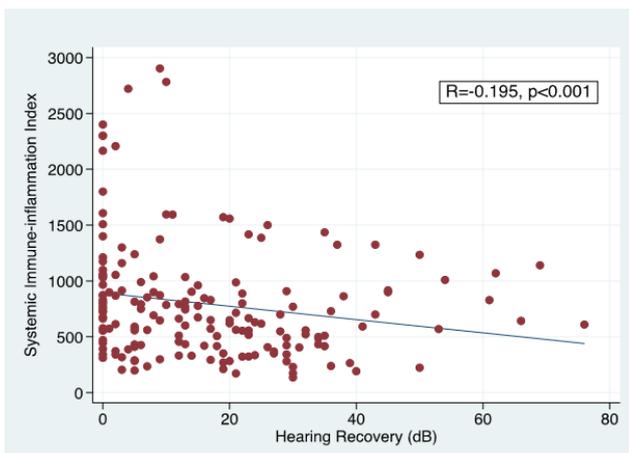


Figure 3: Correlation between hearing loss recovery and systemic immune-inflammation index

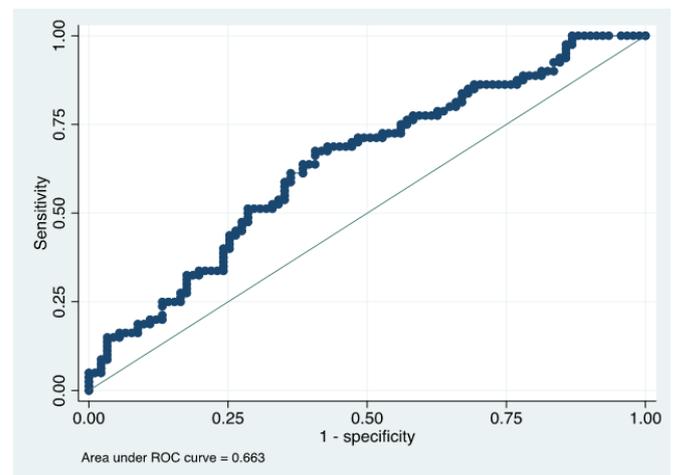


Figure 4: Receiver operating characteristic curves of hearing loss recovery

including diabetes mellitus and hypertension, cannot be determined due to the retrospective nature of study. Second, SII was not compared with other inflammatory markers, such as CRP, fibrinogen, or myeloperoxidase, because of the retrospective nature of our study. As a result of these limitations, our results may not apply to all ISSHL patients.

Conclusion

In conclusion; SII, an easily available and relatively cheap marker, was associated with the severity of hearing loss. In addition, this index was also associated with the recovery of hearing loss. To the best of our knowledge, this is the first and largest study showing that a high SII value, an indicator of an increased inflammation, was associated with severe hearing loss and also worse sign of recovery.

Disclosure Statement: The authors declare that there are no conflicts of interest.

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