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Evaluation of the immature granulocyte count in idiopathic sudden sensorineural hearing loss

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ABSTRACT

Aims: The purpose of our study was to show whether the immature granulocyte count (IGC) can be used as a prognostic marker in idiopathic sudden sensorineural hearing loss (ISSNHL).

Methods: This study is a retrospective case-control clinical study. Patients presenting to our clinic between June 2019 and June 2022, diagnosed with ISSNHL, and receiving the same treatment protocol were investigated. Preoperative complete blood count values of 40 normal individuals with normal hearing who presented to our clinic due to nasal septum deviation were adopted as the control group. Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) (platelet×neutrophil/lymphocyte) values were calculated in addition to IGC values in complete blood counts from the patient and control groups. The patient group was classified into treatment-responsive and non-responsive subgroups according to the results of audiological examinations performed after one month based on Siegel's criteria. IGC, SII, NRL, and PLT values were compared between all groups.

Results: Comparison of the patient and control group's complete blood count data revealed higher leukocyte and neutrophil counts, IGC and also NLR, PLR, and SII values in the patient group compared to the control group. However, lymphocyte counts were lower in the patient group. None of the parameters previously emerging as significant in the data of patients with healing and non-healing idiopathic sudden hearing loss were statistically significant, and IGC is of no prognostic value in ISSNHL.

Conclusion: IGC may be a novel and inexpensive indicator of ISSNHL and one easily determined with complete blood count, but it is of no prognostic value in the disease.

Keywords: Idiopathic sudden sensorineural hearing loss, immature granulocyte, prognosis

INTRODUCTION

Idiopathic sudden sensorineural hearing loss (ISSNHL) is an acute, unilateral, sensorineural loss of hearing with no definite cause involving sudden onset loss of hearing, greater than 30 decibels (dB) at three consecutive frequencies, usually within three days.[1,2]

The etiology of ISSNHL is not yet fully understood. Prognostic indicators and biomarkers are therefore important for appropriate treatment selection. Studies have shown that parameters such as hypertension, hyperlipidemia, diabetes mellitus, presence of metabolic syndrome, advanced age, delayed treatment, vertigo, alcohol, vasculopathy and hearing loss at high frequencies adversely affect prognosis,[3-5] while younger age, having tinnitus and early treatment have a positive impact on prognosis.[6]

Various different approaches have been recommended in the treatment of ISSNHL, such as steroids, hyperbaric oxygen, vasodilator agents, antiviral agents, and diuretics, although treatment remains controversial. In addition, spontaneous recovery at rates of up to 60% may occur in ISSNHL without treatment.[7] This means that greater efforts are required to identify prognostic factors or factors affecting the nature of the disease for the treatment of ISSNHL.

The neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and Systemic Immune Inflammation Index (SII) (platelet×neutrophil/lymphocyte) can be easily calculated from peripheral complete blood counts. Various hematological indices, such as NLR and PLR have recently been found to be associated with prognosis in patients with ISSNHL.[8] These have also been shown to be capable of use as inflammatory markers.[9]

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Immature granulocytes (IGs) consisting of promyelocytes, myelocytes and metamyelocytes are not present in peripheral blood under normal physiological conditions.[10] However, the immature granulocyte count (IGC) in peripheral blood can indicate bone marrow activation in periods of infection and inflammation.[11] IGC is easy to obtain in complete blood counts with automatic hematological analyzers. There are studies in the literature showing that IGC increases earlier than CRP and leukocyte count in inflammatory conditions such as sepsis and infection.[10,11]

We encountered no previous studies investigating the relationship between ISSNHL and the IGC. The purpose of our study was therefore to investigate the prognostic value of the IGC in ISSNHL.

METHODS

This retrospective study was performed in accordance with the principles of the Declaration of Helsinki. Approval of the study was received from Kastamonu University Clinical Researches Ethics Committee (Date: 06.07.2022, Decision No: 2022-KAEK-38). Patients aged 18-65 presenting to our clinic between June 2019 and June 2022, diagnosed with ISSNHL, and treated and follow-up on an outpatient basis were included.

The inclusion criteria were sensorineural hearing loss of at least 30 decibels (dB) at three consecutive frequencies within three days, presentation within a week of onset, no previous steroid use, blood specimens being collected at the first presentation, pure tone hearing tests being performed, and no abnormal findings that would cause loss of hearing at magnetic resonance imaging. Patients with any previous otological disease, history of acoustic trauma, any acute inflammation, hypertension, coronary diseases, chronic obstructive pulmonary disease, renal diseases, connective tissue diseases, liver diseases, diabetes mellitus or regularly taking medications for any disease were excluded from the study. Pre-operative complete blood count specimens from 40 individuals with no health problems who presented to the ear, nose, and throat clinic due to nasal septum deviation and with normal hearing were employed as the control group. There was no significant age or sex difference between the patient and control group.

All patients' complete blood count and pure tone audiometry thresholds at 250, 500, 1000, 2000, 4000, and 8000 Hz before and after treatment were recorded. All patients were evaluated according to their recovery status during a one-month follow-up period. All were started on 1 mg/kg oral methylprednisolone, treatment being completed in 14 days with gradual dose reductions. Siegel's hearing recovery criteria were used to assess the patients' response to treatment (Table 1). According to these criteria, types 1, 2 and 3 were defined as the recovery group and type 4 was defined as the non-recovery group.

Table 1. Siegel's criteria

Type	Description	Details
1.	Complete recovery	Final hearing level 25 dB
2.	Partial recovery	More than 15 dB hearing gain dB and a final haring level of 25-45 dB
3.	Slight recovery	More than 15 dB hearing gain and a final hearing level >45 dB
4.	No recovery	Hearing gain less than 15 dB

Statistical Analysis

This study data were retrieved from the hospital information management system. Complete blood count parameters in the patient group and control group requested at the time of presentation to hospital and measured using an XN-1000 (Sysmex Corporation, Kobe, Japan) automatic hematological analyzer were examined retrospectively. NLR, PLR, SII, IGC, and IG% values were analyzed in addition to standard complete blood count parameters. Blood specimens from the patient group (39) were subsequently subjected to statistical comparisons between those with (23) and without recovery (16).

This study data were analyzed on Statistical Package for Social Sciences version 18.0 for Windows software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as median (25^{th}-75^{th} percentiles) for numerical variables, number and percentage for categorical variables. Since the results were not normally distributed, the Mann-Whitney U test was applied in the comparison of data between the control and ISSNHL groups and the recovery and non-recovery subgroups. The chi-square test was applied to determine whether there was any gender difference between groups. Area under the curve (AUC), cut-off, sensitivity and specificity values were determined by receiver operating characteristic (ROC) analysis and Youden index. p value <0.05 were regarded as statistically significant (Figure).

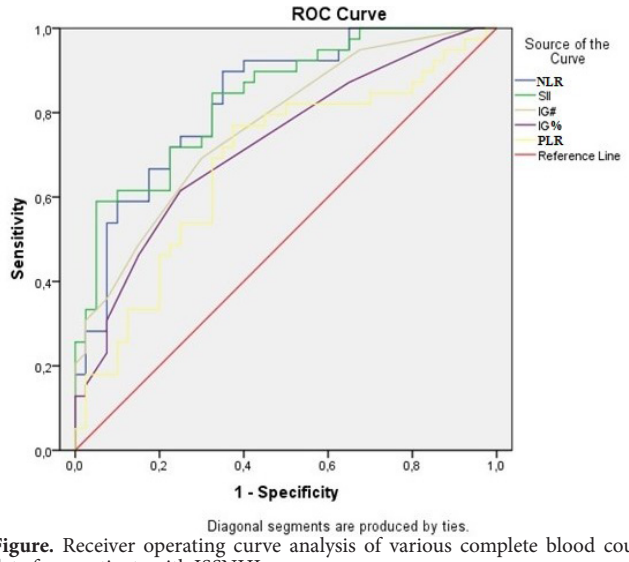

Figure. Receiver operating curve analysis of various complete blood count data from patients with ISSNHL

ROC: Receiver operating characteristic, ISSNHL: Idiopathic sudden sensorineural hearing loss, NLR: Neutrophil lymphocyte ratio, SII: Systemic Immune Inflammation Index, PLR: Platelet lymphocyte ratio

RESULTS

Comparison revealed higher IG, leukocyte, and neutrophil counts, as well as NLR, PLR, and SII values in the patient group than in the control group, while lymphocyte counts were lower than in the control group (Table 2).

SII and NLR were found to be of high predictive value in distinguishing the idiopathic sudden hearing loss and control groups. Additionally, IGC, IG%, and PLR exhibited moderate predictive value (Table 3).

None of the parameters previously reported to be significant in the data for recovering and non-recovering patients emerged as statistically significant, and IGC was of no prognostic value in ISSNHL (Table 4).

Table 2. A comparison of the patient and control groups

	Control (40)	Patient (39)	
	Median (IQR)		p
WBC (×10³/µl)	7.1 (5.4, 7.9)	8.7 (7.4, 11.0)	<0.001
NEU# (×10³/µl)	3.6 (2.6, 4.3)	5.7 (4.1, 7.2)	<0.001
LYM# (×10³/µl)	37.6 (32.3, 45.1)	25.1 (21.6, 33.5)	<0.001
IG# (×10³/µl)	0.02 (0.01, 0.03)	0.03 (0.02, 0.06)	<0.001
IG (%)	0.3 (0.2, 0.37)	0.4 (0.3, 0.6)	<0.001
NLR	1.3 (1.0, 1.7)	2.6 (1.6, 3.3)	<0.001
PLR	102 (90, 126)	126 (112, 151)	0.006
SII	391 (257, 545)	726 (460, 1101)	<0.001

WBC: White blood count, LYM: Lymphocyte, IG: Immature granulocyte, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, SII: Systemic Immune Inflammation Index

Table 3. Receiver operating curve analysis of various complete blood count data from patients with ISSNHL

	Cut-off	AUC	95% CI	p	Sensitivity%	Specificity%
SII	638	0.835	0.74-0.92	<0.001	59	95
NLR	Oca.53	0.830	0.75-0.92	<0.001	90	65
IGC	0.025	0.768	0.67-0.87	<0.001	69	70
IG%	0.035	0.725	0.61-0.84	0.001	62	75
PLR	112	0.680	0.56-0.80	0.006	77	63

ISSNHL: Idiopathic sudden sensorineural hearing loss, AUC: Area under the curve, SII: Systemic Immune Inflammation Index, NLR: Neutrophil lymphocyte ratio, IGC: Immature granulocyte count, IG: Immature granulocyte, PLR: Platelet lymphocyte ratio

Table 4. A Comparison of the recovering and non-recovering idiopathic hearing loss groups

	Recovery (23)	Non-recovery (16)	p
	Median (IQR)		
WBC (×10³/µl)	8.28 (7.01, 9.75)	9.93 (8.09, 11.2)	0.077
NEU# (×10³/µl)	5.5 (3.9, 6.07)	6.5 (4.7, 8.9)	0.127
LYM# (×10³/µl)	2.1 (1.7, 2.7)	2.3 (1.5, 2.6)	0.597
IGC (×10³/µl)	0.03 (0.02, 0.05)	0.04 (0.03, 0.09)	0.093
IG (%)	0.4 (0.3, 0.6)	0.5 (0.3, 0.6)	0.165
NLR	2.6 (1.8, 3.1)	2.5 (1.6, 4.9)	0.886
PLR	130 (106, 142)	121 (115, 199)	0.954
SII	726 (444, 889)	797 (497, 1607)	0.356

WBC: White blood count, LYM: Lymphocyte, IGC: Immature granulocyte count, IG: Immature granulocyte, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, SII: Systemic Immune Inflammation Index

DISCUSSION

The purpose of our study was to investigate the importance of IG and various other blood count parameters (WBC, neutrophil count, NLR, PLR, and SII) as predictive and prognostic markers in ISSNHL. Both IGC and other hematological markers were significantly higher in the patients with ISSNHL than in the healthy control group, but none was of any prognostic value.

The etiology of SSINHL is not yet fully understood, but it is thought to be multifactorial. Various mechanisms have been proposed that may contribute to cochlear damage, such as viral infection, vascular disorders, immune-mediated mechanisms, and inflammation.[12] However, there is no definite evidence for any specific hypothesis. Some studies have shown an association between ISSNHL and chronic inflammation.[13] Chronic inflammation is thought to be a risk factor in the development of atherogenesis and microvascular damage, which increase the risk of cochlear ischemia and induce endocochlear immune responses.[14-16] Vascular wall damage increases the risk of ischemia in chronic inflammation and this is important for cochlea supplied by a single artery.[14] Systemic steroid therapy represents the basis of treatment in ISSNHL. However, no improvement has been observed in 20-50% of patients despite two-week oral or intravenous steroid therapy.[15]

WBC and various subtypes are used as inflammatory markers. NLR and PLR values are newly identified inflammatory markers that can be calculated from peripheral blood specimens. Elevation in NLR values is associated with the level of inflammation,[5] while high PLR values are indicative of atherosclerosis.[17] The SII can be used as an inflammatory marker in malignancy and inflammatory states. Some studies have reported that it represents a superior index of systemic inflammation than NLR and PRL values.[18,19] IGs are not present in peripheral blood under normal physiological conditions. Peripheral IGC can indicate increased bone marrow activation in periods of infection and inflammation. This has been shown to rise earlier than CRP and leukocyte counts in infection and sepsis.[10,11] In some studies, significant IGC elevation has been observed in acute appendicitis and pancreatitis.[10]

In this study, both IGC values and NRL, PRL and SII values were higher in patients with ISSNHL than in the control group. No statistically significant difference was observed in IG, NRL, PRL, or SII values between patients with recovery of at least 15 dB according to Siegel's criteria and patients with no recovery. This finding confirms that inflammation is important in the pathogenesis of ISSNHL and supports the idea that IGs are of predictive value in ISSNHL. However, neither IGs nor the SII were of any prognostic significance in ISSNHL.

Our review of the literature revealed no previous studies concerning IGC in patients with hearing loss. However, the NLR and PLR indices have been widely investigated in ISSNHL. Masuda et al.[16] reported that increases in neutrophil counts are an indicating poor prognosis in ISSNHL. Özler[20] reported that NRL was higher in patients with ISSNHL than in the control group. SEO et al.[17] reported that NRL and PRL values were higher in patients with ISSNHL than in the control group. There are studies in the literature reporting that increased NRL values are associated with poor prognosis in ISSNHL.[21,22] In contrast, in a prospective study, Gupta et al.[23] determined no a statistically significant association between the severity of hearing loss in patients with ISSNHL and hematological tests (total leukocyte count and subtypes) and reported no relationship between NRL values and recovery. The number of studies of the prognostic value of the SII in ISSNHL is limited. Ulu et al.[24] reported that the SII, a novel index, may represent an indicator in ISSNHL and is also capable of predicting prognosis. In their retrospective study, Kumbul et al.[25] reported high SII values in patients with ISSNHL, but that it exhibited no prognostic value. We think that the fact that the majority of these studies are retrospective, their low patient numbers, the lack of any universally accepted threshold values for NRL and PRL levels, the use of different criteria to define recovery, the presence or absence of additional diseases that might cause inflammation in patients with ISSNHL, and the use of different devices such as hematological analyzers and audiometers in studies may account for the heterogeneity in the results obtained.

Limitations

To our knowledge, our study is the first study to investigate the prognostic significance of the IGC in ISSNHL and to investigate it to support the role of inflammation in the pathogenesis of ISSNHL.

The limitations of our study are its single-center nature and limited patient numbers. In our study, finding that IGC, NRL and SII values were significantly higher in patients with ISSNHL compared to the healthy control group supports the idea of the involvement of inflammation in the etiopathogenesis in ISSNHL. However, the absence of any significant difference in these values between the recovering and non-recovering patients show that they are of no prognostic significance. Early treatment is important in ISSNHL. Prognostic factors and alternative treatments (hyperbaric oxygen, vasodilator agents, antiviral agents, etc.) should also be considered in addition to standard cortisone therapy at the beginning of treatment.

CONCLUSION

Recently, new inflammatory markers have described to predict inflammatory states. IGC may be a novel and inexpensive indicator of ISSNHL and one easily determined from complete blood count, but it is of no prognostic value in ISSNHL. Nonetheless, in the light of the study limitations, we think that further prospective studies including various inflammatory factors such as CRP, fibrinogen, cytokines, and interleukins in larger numbers of patients with ISSNHL are needed to confirm our findings.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Kastamonu University Clinical Researches Ethics Committee (Date: 06.07.2022, Decision No: 2022-KAEK-38).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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