The Journal of International Advanced Otology

Int Adv Otol 2014; 10(3): 197-200 • DOI: 10.5152/iao.2014.76

Original Article

New Inflammation Parameters in Sudden Sensorineural Hearing Loss: Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio

Aykut İkincioğulları, Sabri Köseoğlu, Murat Kılıç, Doğan Atan, Kürşat Murat Özcan, Mehmet Ali Çetin, Serdar Ensari, Hacı Hüseyin Dere

Department of Ear Nose and Throat, Ankara Numune Education and Research Hospital, Ankara, Turkey (AI, SK, MK, DA, KMO, MAC, SE, HHD)

OBJECTIVE: The etiopathogenesis of sudden sensorineural hearing loss (SSNHL) is not clearly defined. Inflammation is being emphasized in its etiology. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are the parameters that show inflammation that can be obtained easily without additional cost. In this study, we aimed at delineating the relationship between SSNHL and the inflammation markers NLR and PLR.

MATERIALS and METHODS: This study was performed with 102 patients diagnosed with SSNHL and 119 sex- and age-matched controls. All subjects in the study and the control group had their complete blood count (CBC) results, which were evaluated retrospectively to calculate NLR and PLR values. All patients underwent an audiological examination on the 1st, 3rd, 10th, and 30th days of the hearing loss. All patients received 1 mg/kg IV prednisolone treatment in tapered amounts to be completed in 15 days. Based on the improvements seen in the audiograms, the patients were divided into two groups: responders and non-responders to treatment.

RESULTS: PLR and NLR values of the patient group were significantly higher than in the control group ($p<0.001$, $p<0.001$). Furthermore, patients who responded to treatment had significantly higher NLR values than those who did not respond ($p=0.010$).

CONCLUSION: In this study, NLR and PLR values were found to be significantly high in SSNHL patients. PLR value was investigated for the first time in the literature in SSNHL patients. NLR and PLR values are parameters that aid in the diagnosis of SSNHL. Moreover, SSNHL patients who had higher NLR values responded to the treatment better.

KEY WORDS: Sudden hearing loss, inflammation, platelets, lymphocytes, neutrophils

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is generally defined as sensorineural hearing loss of 30-dB or more in three consecutive frequencies within 3 days [1, 2]. SSNHL is one of the emergencies encountered in ear, nose and throat (ENT) practice. Therefore, early diagnosis and treatment are important. A detailed history and physical examination for the differential diagnosis of other causes of hearing loss and the presence of sensorineural hearing loss in the audiological examination establish the diagnosis. For the differential diagnosis of pathologies, like acoustic neuroma, that might lead to sensorineural hearing loss, magnetic resonance imaging (MRI) can be used.

The etiology of SSNHL includes vascular, viral, and immune theories. However, its etiopathogenesis has not yet been clearly delineated [3-6]. In studies performed during recent years, systemic stress and inflammation have mainly been held responsible [7-9]. The widespread use of steroids in treatment supports this theory.

The ratio of neutrophils to lymphocytes (NLR) and that of platelets to lymphocytes (PLR) can be calculated with a simple hemogram analysis of a peripheral blood sample. PLR values are found to be high in various peripheral vascular diseases, coronary artery diseases, and certain gynecological and hepatobiliary malignancies, and this has been related with a poor prognosis. NLR increases during systemic inflammation, certain gynecological and gastrointestinal cancers, and some cardiovascular diseases [10-12]. In a recent study, the NLR values of SSNHL patients were found to be high, which was reported as a poor prognostic indicator [13].

In the literature, we could not come across any study that delineated the correlation between SSNHL and PLR. In this study, we aimed at identifying the possible diagnostic and prognostic correlation between NLR, PLR, and SSNHL.

Corresponding Address:
Sabri Köseoğlu, Department of Ear Nose and Throat, Ankara Numune Education and Research Hospital, Ankara, Turkey
Phone: +90 505 645 99 11; E-mail: drskoseoglu@gmail.com

Submitted: 06.11.2014 **Accepted:** 10.11.2014

MATERIALS and METHODS

The study included 102 patients diagnosed with and treated for SSNHL from 2005 to 2013 and 119 age- and sex-matched controls. In the study and the control groups, patients with inner ear pathologies that might lead to hearing loss (Meniere's disease, autoimmune inner ear disease, Cogan syndrome, otosyphilis, etc.), middle ear pathologies (acute otitis media, chronic otitis media, otosclerosis, etc.), and external ear pathologies (external auditory canal osteoma, exocytosis, and otitis externa, etc.) were excluded from the study. Furthermore, patients with systemic diseases, like uncontrolled diabetes mellitus, uncontrolled hypertension, acute coronary artery disease, connective tissue disease in active stage, vasculitis, inflammatory bowel disease, chronic renal failure, and chronic liver failure, were excluded, as well. All patients diagnosed with SSNHL were hospitalized. Complete blood count (CBC), detailed biochemical parameters, serum lipids, thyroid hormone levels, and hepatitis markers were studied on the day of hospitalization, before the initiation of any medical treatment, such as steroids. Furthermore, contrast temporal MRI examination was performed for the differential diagnosis of intracranial and inner ear pathologies. Audiological examinations were performed on the first, third, tenth, and thirtieth day of admission. Audiological examinations were performed with brand audiometry device (AC 40; Interacoustics, Denmark) by the same audiologist and audiometrist team. The hearing thresholds of the patients at 250, 500, 1000, 2000, 4000, and 8000 Hz were recorded. All patients received prednisolone treatment at a beginning dose of 1 mg/kg IV, which was tapered off in 15 days. Patients also received 12 g/day IV piracetam. Patients with a recent history of viral infection also received antiviral treatment (acyclovir 1000 mg/day).

Complete blood count parameters were analyzed with hematology analyzer (Sysmex XE-2100; Kobe, Japan), and hemoglobin, erythrocyte, leukocyte, neutrophil, lymphocyte, platelet counts, and PLR and NLR values were calculated.

Patients were divided into 3 groups according to the response to treatment [14].

Total recovery: Pure-tone average (dB) within 10 dB of initial hearing level or within 10 dB of the hearing level of the unaffected ear

Partial recovery: Pure-tone average (dB) within 50% of initial hearing level or greater than 10 dB improvement of hearing level

No recovery: Less than 10 dB improvement in hearing level relative to the initial hearing level

Subsequently, patients with total and partial recovery were defined as responders, and the others were non-responders.

Statistical Analysis

All statistical analyses of data were carried out using Statistical Package for the Social Sciences (SPSS) software (IBM Corporation; USA) Descriptive statistical methods (mean, standard deviation) were used for the evaluation of data. To determine the significance of the differences between two groups, independent t-test and the Mann-Whitney U-test were used. Kruskal-Wallis test was used for the comparison of differences between groups. Spearman and Pearson correlation analysis was used for the correlation analysis to test the relationship of continuous data. Differences were considered significant at $p<0.05$.

Table 1. Patients charecteristics and complete blood count parameters

		Patients	Control	P value
Age		48.94±13.86	47±9.63	0.200
Gender	Male	54	65	
	Female	48	54	0.256
NLR		4.02±3.57	1.32±0.22	<0.001
PLR		148.595±70.553	95.298±25.509	<0.001
WBC		9.07±2.87	7.33±1.60	0.583
Neutrophil		6.41±3.01	3.69±1.69	0.004
Lymphocyte		2.09±0.95	2.83±0.02	0.547
Platelet		263274±64108	259321±64797	0.844

NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; WBC: white blood cells

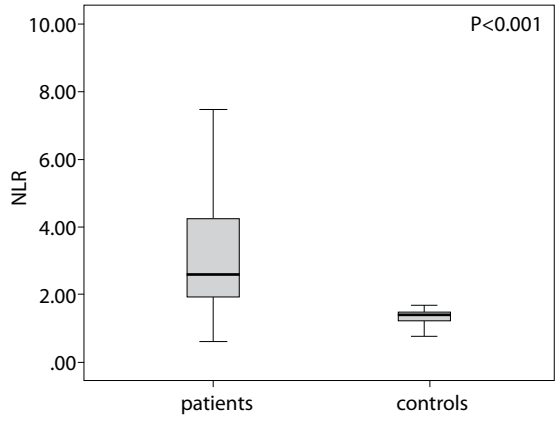

Figure 1. The neutrophil-to-lymphocyte ratio values of patient and control groups
NLR: neutrophil-to-lymphocyte ratio

RESULTS

The mean age of the patient group was 48.94±13.86 years, while that of the control group was 47±9.63. The male-to-female ratio was 54/48 in the patient group and 65/54 in the control group. The patient and control groups had similar distributions with regard to age and sex. Characteristic features and hemogram analyses of the patient and control groups are summarized in Table 1.

The mean NLR value was 4.02±3.57 for the patient group and 1.32±0.22 for the control group, which is statistically significant ($p<0.001$) (Figure 1). Neutrophil count was significantly higher in the patient group ($p=0.004$). The patient and control groups did not differ significantly in terms of their lymphocyte counts ($p=0.547$).

The mean PLR value of the patient group was 148.595±70.553 and 95.298±25.509 for the control group, and the difference was statisti-

Table 2. Complete blood count parameters of responders and nonresponders groups

	Responders	Nonresponders	P value
n	62(60.8%)	40(39.2%)	-
WBC	9.67±3.03	8.15±2.33	0.019
Neutrophil	7.12±3.09	5.31±2.20	0.007
Lymphocyte	2.07±1.09	2.11±0.67	0.380
Platelet	268032±64373	255900±62546	0.384
NLR	4.68±3.72	3.00±2.10	0.010
PLR	158.625±78.240	133.048±54.458	0.136

NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; WBC: white blood cells
Responders: Pure-tone average (PTA) (dB) within 10 dB hearing levels of initial hearing level or within 10 dB of the hearing level of the unaffected ear and pure-tone average (dB) within 50% of initial hearing level or greater than 10-dB improvement of the hearing level (total recovered + partial recovered groups)
Nonresponders: Less than 10 dB improvement in hearing level relative to the initial hearing level (Unrecovered group)

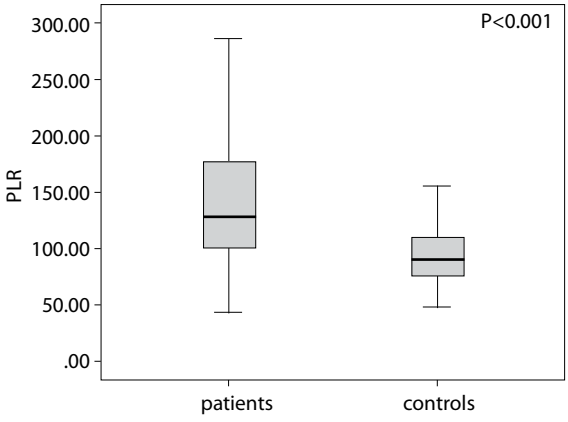

Figure 2. The platelet-to-lymphocyte ratio values of patient and control groups.
PLR: platelet-to-lymphocyte ratio

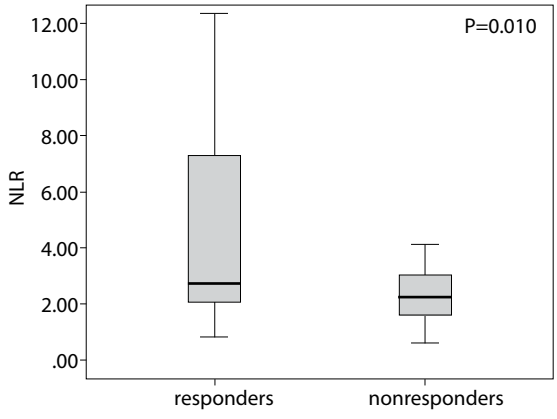

Figure 3. The neutrophil-to-lymphocyte ratio values of responders and non-responders.
NLR: neutrophil-to-lymphocyte ratio
Responders: Pure-tone average (dB) within 10 dB of initial hearing level or within 10 dB of the hearing level of the unaffected ear and pure-tone average (dB) within 50% of initial hearing level or greater than 10 dB improvement of hearing level (total recovered + partial recovered groups)
Non-responders: Less than 10 dB improvement in hearing level relative to the initial hearing level (unrecovered group)

cally significant (p<0.001) (Figure 2). Platelet counts were found to be similar in both groups (p=0.844).

In terms of responders and non-responders to treatment, mean NLR values were 4.68±3.72 and 3.00±2.10, respectively, and the difference was statistically significant (p=0.01) (Figure 3). When PLR values were compared based on treatment responses, the mean PLR value of the patients who responded to treatment was 158.625±78.240, and that of non-responders was 133.048±54.458; this difference was not statistically significant (p=0.136) (Table 2).

No correlation could be established between NLR and PLR values and the elapsed time between the start of the hearing loss and patient admission (p=0.577, p=0.605).

DISCUSSION

The etiopathogenesis of SSNHL has not yet been clearly understood. Systemic stress and inflammation have been underlined in studies performed during recent years [7-9]. White blood cells (WBCs) and the number of their subgroups increase especially during cardiovascular diseases and are used as inflammatory markers [15]. Masuda et al. [9] reported that the increase in neutrophil count was correlated with a poor prognosis for SSNHL patients. Studies performed with inflammatory cytokines, like TNF alpha, interleukin 6, and interleukin 10, demonstrated that these cytokines were not correlated with SSNHL [16, 17].

Neutrophil-to-lymphocyte ratio (NLR) is calculated by dividing the neutrophil count obtained from the CBC analysis by the lymphocyte count. PLR is calculated in a similar manner by dividing the platelet count by the lymphocyte count. Since both NLR and PLR values can be calculated based on a routine hemogram and do not require any additional cost, it is a low-cost test that can be easily implemented.

Neutrophil-to-lymphocyte ratio is used as a marker showing systemic inflammation [18]. In addition to vascular pathologies, like ischemic cerebrovascular occlusive and acute coronary diseases, NLR also increases during inflammatory diseases, like SSNHL and Bell's palsy [10, 13, 15, 19, 20]. In this study, NLR values prior to initiation of steroid therapy were statistically higher in SSNHL patients than in controls. Likewise, in a study performed by Ulu et al. [20] on SSNHL patients, the mean NLR value was found to be statistically higher in the patient group. In this study, the mean NLR value was 3.96±2.95, while in our study, it was 4.02±3.57. Ulu et al. [20] reported that the NLR value was correlated with an unfavorable prognosis. Different from that study, in our study, the patients who responded to treatment had a mean NLR value of 4.68±3.72, which was significantly higher than that of those who did not respond to treatment (3.00±2.10). We concluded that in our study, patients with higher NLR values had a better response to treatment. Several theories are being put forward on the etiopathogenesis of SSNHL. The NLR value was found to be higher in SSNHL patients who have a predominance of inflammatory factors in their etiology, and they benefited more from the anti-inflammatory treatment (systemic steroids) that was used. In other words, it is possible to foresee that the higher the inflammation marker NLR is, the greater the benefit obtained from the steroid treatment is. This finding should be further investigated with studies having larger patient groups.

Platelet-to-lymphocyte ratio was investigated for the first time in SSNHL patients in this study. Similar to NLR, PLR is also an inflammatory marker that can be studied without any additional cost. In various diseases like myocardial infarction, critical limb ischemia, end-stage renal failure, and ovarian epithelial carcinoma, PLR value can be used as an inflammatory marker and can be correlated with poor prognosis [21-24]. Especially, in new studies performed during recent years, PLR value was reported to correlate with end-organ damage and high morbidity in non-ST myocardial infarction and peripheral vascular diseases [21, 25]. In this study, PLR values prior to initiation of steroid treatment were found to be significantly higher in SSNHL patients compared to controls. When the levels of this marker were studied in responder and non-responder groups, no correlation was found with recovery.

The study has a limitation regarding the absence of a cut-off value for NLR and PLR. If the study had been designed with a larger study group, it might have been possible to determine a cut-off value for NLR and PLR, predicting the diagnosis and prognosis of SSNHL.

In conclusion, values of the inflammatory markers NLR and PLR were found to be significantly higher in SSNHL patients in this study. The correlation between PLR value and SSNHL was shown for the first time in the literature. Moreover, SSNHL patients with higher NLR values were found to have a better response to treatment. NLR and PLR ratios are inexpensive and easy to obtain and therefore should be used as helpful diagnostic tools in all patients considered to have SSNHL.

Ethics Committee Approval: Ethics committee approval was not received due to the retrospective nature of this study.

Informed Consent: Written informed consent was not obtained due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.I., S.K., M.A.C.; Design - A.I., D.A., K.M.O.; Supervision - S.E., H.H.D.; Materials - A.I., S.K., M.K., K.M.O.; Data Collection and/or Processing - A.I., S.K., M.K., M.A.C.; Analysis and/or Interpretation - D.A., M.A.C., K.M.O.; Literature Review - S.K., M.K., D.A.; Writer - A.I., S.K.; Critical Review - S.E., H.H.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial sport.

REFERENCES

1. Garcia Berrocal JRG, Ramirez-Camacho R, Portero F, Vargas JA. Role of viral and Mycoplasma pneumoniae infection in idiopathic sudden sensorineural hearing loss. Acta Otolaryngol 2000; 120: 835-9. [CrossRef]
2. Loughran S. Management of sudden sensorineural hearing loss: a consultant survey. J Laryngol Otol 2000; 114: 837-9. [CrossRef]
3. Hatano M, Uramoto N, Okabe Y, Furukawa M, Ito M. Vitamin E and vitamin C in the treatment of idiopathic sudden sensorineural hearing loss. Acta Otolaryngol 2008; 128: 116-21. [CrossRef]
4. Merchant SN, Durand ML, Adams JC. Sudden deafness: is it viral? ORL J Otorhinolaryngol Relat Spec 2008; 70: 52-60. [CrossRef]
5. Quaranta N, Ramunni A, Brescia P, D'Elia A, Vacca A, Ria R. Soluble intercellular adhesion molecule 1 and soluble vascular cell adhesion molecule 1 in sudden hearing loss. Otol Neurotol 2008; 29: 470-4. [CrossRef]
6. Ryan AF, Harris JP, Keithley EM. Immune-mediated hearing loss: basic mechanisms and options for therapy. Acta Otolaryngol Suppl 2002; 38-43. [CrossRef]
7. Greco A, Fusconi M, Gallo A, Marinelli C, Macri GF, De Vincentiis M. Sudden sensorineural hearing loss: an autoimmune disease? Autoimmun Rev 2011; 10: 756-61. [CrossRef]
8. Hiramatsu M, Teranishi M, Uchida Y, Nishio N, Suzuki H, Kato K, et al. Polymorphisms in genes involved in inflammatory pathways in patients with sudden sensorineural hearing loss. J Neurogenet 2012; 26: 387-96. [CrossRef]
9. Masuda M, Kanzaki S, Minami S, Kikuchi J, Kanzaki J, Sato H, et al. Correlations of inflammatory biomarkers with the onset and prognosis of idiopathic sudden sensorineural hearing loss. Otol Neurotol 2012; 33: 1142-50. [CrossRef]
10. Bhat T, Teli S, Rijal J, Bhat H, Raza M, Khoueiry G, et al. Neutrophil to lymphocyte ratio and cardiovascular diseases: a review. Expert Rev Cardiovasc Ther 2013; 11: 55-9. [CrossRef]
11. Proctor MJ, McMillan DC, Morrison DS, Fletcher CD, Horgan PG, Clarke SJ. A derived neutrophil to lymphocyte ratio predicts survival in patients with cancer. Br J Cancer 2012; 107: 695-9. [CrossRef]
12. Wang D, Yang JX, Cao DY, Wan XR, Feng FZ, Huang HF, et al. Preoperative neutrophil-lymphocyte and platelet-lymphocyte ratios as independent predictors of cervical stromal involvement in surgically treated endometrioid adenocarcinoma. Onco Targets Ther 2013; 6: 211-6.
13. Bucak A, Ulu S, Oruc S, Yucedag F, Tekin MS, Karakaya F, et al. Neutrophil-to-lymphocyte ratio as a novel-potential marker for predicting prognosis of Bell palsy. Laryngoscope 2014; 124: 1678-81. [CrossRef]
14. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. Arch Otolaryngol 1980; 106: 772-6. [CrossRef]
15. Arruda-Olson AM, Reeder GS, Bell MR, Weston SA, Roger VL. Neutrophilia predicts death and heart failure after myocardial infarction: a community-based study. Circ Cardiovasc Qual Outcomes 2009; 2: 656-62. [CrossRef]
16. Demirhan E, Eskut NP, Zorlu Y, Cukurova I, Tuna G, Kirkali FG. Blood levels of TNF-α, IL-10, and IL-12 in idiopathic sudden sensorineural hearing loss. Laryngoscope 2013; 123: 1778-81. [CrossRef]
17. Haubner F, Martin L, Steffens T, Strutz J, Kleinjung T. The role of soluble adhesion molecules and cytokines in sudden sensorineural hearing loss. Otolaryngol Head Neck Surg 2011; 144: 575-80. [CrossRef]
18. Teo M, Mohd Sharial MS, McDonnell F, Conlon KC, Ridgway PF, McDermott RS. Prognostic role of neutrophil-to-lymphocyte ratio in advanced pancreatic ductal adenocarcinoma: impact of baseline fluctuation and changes during chemotherapy. Tumori 2013; 99: 516-22.
19. Celikbilek A, Ismailogullari S, Zararsiz G. Neutrophil to lymphocyte ratio predicts poor prognosis in ischemic cerebrovascular disease. J Clin Lab Anal 2014; 28: 27-31. [CrossRef]
20. Ulu S, Ulu MS, Bucak A, Ahsen A, Yucedag F, Aycicek A. Neutrophil-to-lymphocyte ratio as a new, quick, and reliable indicator for predicting diagnosis and prognosis of idiopathic sudden sensorineural hearing loss. Otol Neurotol 2013; 34: 1400-4. [CrossRef]
21. Azab B, Shah N, Akerman M, McGinn JT Jr. Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. J Thromb Thrombolysis 2012; 34: 326-34. [CrossRef]
22. Henriques A, Rodriguez-Caballero A, Nieto WG, Langerak AW, Crido I, Lecrevisse Q, et al. Combined patterns of IGHV repertoire and cytogenetic/molecular alterations in monoclonal B lymphocytosis versus chronic lymphocytic leukemia. PLoS One 2013; 8: e67751. [CrossRef]
23. Raungkaewmanee S, Tangjitgamol S, Manusirivithaya S, Srijaipracharoen S, Thavaramara T. Platelet to lymphocyte ratio as a prognostic factor for epithelial ovarian cancer. J Gynecol Oncol 2012; 23: 265-73. [CrossRef]
24. Turkmen K. Platelet-to-lymphocyte ratio: one of the novel and valuable platelet indices in hemodialysis patients. Hemodial Int 2013; 17: 670.
25. Gary T, Pichler M, Belaj K, Hafner F, Gerger A, Froehlich H, et al. Platelet-to-lymphocyte ratio: a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients. PLoS One 2013; 8: e67688. [CrossRef]