

A Bit Exaggerated Role of Complete Blood Count Parameters on the Prognosis of Idiopathic Sudden Sensorineural Hearing Loss

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Abstract

Idiopathic sudden sensorineural hearing loss (ISSHL) is a commonly seen otorhinolaryngology emergency, and its etiology is still a mystery. In this retrospective clinical study, we aimed to investigate the possible relationship of inflammatory markers derived from CBC such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), Red cell distribution width-to-platelet ratio (RPR), lymphocyte-to-monocyte ratio (LMR), mean platelet volume (MPV) and platelet distribution width (PDW) in ISSHL. A total of 50 idiopathic sudden hearing loss patients were included in the study. They were grouped according to their hearing healing levels as recovered, partially recovered and unrecovered. Also 47 age- and sex- matched healthy individuals created the control group. Their complete blood count parameters of NLR, LMR, PLR, RPR, PDW and MPV were recorded. The results were statistically compared to bring out a significant difference between the groups. There was no significant demographic difference between the groups. The comparison of patient group with control group reveal a significant difference in the NLR, LMR and PDW values ($p < 0.05$). The remaining values were not statistically significant. The analysis of these values according to the recovery level of the ISSHL, there was no statistical difference between the groups ($p > 0.05$). We demonstrated for the first time that LMR value was significantly elevated in ISSHL patients. NLR, LMR, and PDW might be indicative for diagnosis of ISSHL. However, we believe that using these parameters for the screening of the prognosis is a clinically useless exercise.

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Introduction:

Idiopathic sudden sensorineural hearing loss (ISSHL) is one of the emergency conditions of otorhinolaryngology (ORL), defined as 30 decibel (dB) or greater hearing loss at least three consecutive frequencies, occurring in less than 3 days with no identifiable etiology¹. The incidence of ISSHL is 5 - 20 person per 100,000 individuals annually and accounts for 1% of all sensorineural hearing loss cases². Although the existence of different treatment modalities, up to 65% of the cases recovers spontaneously without any treatment³.

In current clinical practice, one of the most frequently ordered laboratory tests is the complete blood count (CBC). In this frequently ordered test, several parameters such as white blood cell, red blood cell and platelet counts and their ratios can be easily evaluated. In recent years, there have been many studies which assess the role of inflammatory and biochemical markers derived from CBC to predict the disease severity or prognosis of coronary artery^{4,5}, liver⁶, renal⁷ and infectious⁸⁻¹⁰ diseases.

In this study, we aimed to investigate the possible relationship of inflammatory markers derived from CBC such as neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW)-to-platelet ratio (RPR), mean platelet volume (MPV) and platelet distribution width (PDW) in ISSHL and to reveal the importance of these parameters in this disease.

Materials and Methods:

Subjects and sample collection.

The 145(85 male, 60 female) patients who were treated for sudden sensorineural hearing loss between

January 2010 and December 2015 at Fatih Sultan Mehmet Education and Research Hospital in Istanbul, Turkey were retrospectively reviewed. The study protocol was approved by the Research Ethical Committee of the Fatih Sultan Mehmet Education and Research Hospital in Istanbul, Turkey as a review (protocol number: 25.04.2016-485).

The patients who were admitted to our clinic in the first week of the start of the hearing loss were only included. Further, the patients who were treated with the standard ISSHL protocol of our clinic which included methylprednisolone in the dose of 1 mg/kg per day, with a progressive dose reduction, maintained for at least two weeks and hyperbaric oxygen therapy (HBO) in a hyperbaric chamber, in which they breathed 100% oxygen at a pressure of 2.5 atmospheres absolute (ATA) once a day for 120 minutes in 10 consecutive daily sessions were included. Other treatment protocols such as intratympanic steroid injections with or without HBO were not taken into consideration.

Patients who had an evidence of a heart disease (such as myocardial infarction, valvular heart disease, congestive heart failure, a history of bypass or percutaneous coronary intervention), autoimmune disease (such as Behçet's Disease, Hashimoto Thyroiditis) or suffered from an acute infection (patients with elevated WBC count (>11,000/mL) or neutrophilia (>70%)), hematological diseases (patients with increased hemoglobin (>18gr/dL) or decreased hemoglobin (<12gr/dL) and other diseases such as sickle cell anemia), coagulopathies (such as Factor V Leiden mutation), intracranial pathologies (hearing loss with cerebrovascular disease, internal acoustic canal mass) and chronic ear diseases (chronic otitis media, otosclerosis, acoustic trauma history, Meniere's disease) were excluded.

Finally, 50 (28 male, 22 female) patients who fulfilled the criteria included to compose the patient group and for the comparison of the CBC parameters, 47 age- and sex- matched healthy individuals whose CBCs were done for regular checkups were included to compose the control group.

Audiometric Evaluation

Hearing assessments of the patients were performed by the same audiometer (Interacoustics AC-40, Denmark) in a quiet cabin. The audiometric examinations were carried out initially and after three weeks of the treatment. If the patient did not recover totally, audiometric examinations were repeated whenever the patient admitted to the ORL policlinic. The average threshold values (dB HL) of 500, 1000, 2000 Hz were used to calculate the arithmetic mean of hearing levels in pure-tone audiometry. Recovery of hearing was classified into 3 groups according to the improvement of hearing levels in the last audiogram of the patients (table 1).

Biochemical and Hematological Analyses

Complete blood count was evaluated using peripheral venous blood samples obtained at the admission of the hospital before the start of treatment. CBC testing was performed using an automated hematology analyzer (CELL-DYN 3700, Abbott, USA) initial to the treatment. The white blood cell (WBC), hemoglobin, hematocrit, platelet, neutrophil, lymphocyte, monocyte, RDW, and PDW counts were recorded and the NLR, LMR, PLR, RPR were calculated from these parameters (table 2). These ratios, MPV and PDW values were compared with the hearing recovery results and the control group.

Statistical Analysis

All statistical calculations were performed with IBM SPSS Statistics version 20.0. Standard descriptive statistical calculations (mean and standard deviation), quantitative comparison of the data and the comparison of normal distribution parameters of the comparison of patient and control groups were assessed with independent-samples Student's T-test, and Mann-Whitney U test was used in the assessment of not normal distributed parameters. To compare the groups according to the hearing levels Kruskal-Wallis test was used. The statistical significance level was established at $p < 0.05$.

Results:

There was no significant demographic difference between the patient and control groups. The mean ages of patient and control groups were 49.50 ± 11.71 and 44.55 ± 14.21 years, respectively. The male-to-female ratios of these groups were 28:22 and 26:21, respectively. The demographic data and mean \pm standard deviation of NLR, LMR, RPR, PLR, MPV, and PDW values of the patient and control groups are listed in table 3. As presented in table 3, mean NLR, LMR and PDW values in patients with ISSHL were significantly different from the controls ($p < 0.05$).

The demographic distribution of patient groups according to the hearing recovery levels are shown in table 4. There were 11 (52.91 ± 9.36 of age) unrecovered, 16 (52.81 ± 10.26 of age) partially recovered and 23 (45.57 ± 12.80 of age) totally recovered patients in these groups. The mean values of NLR, LMR, RPR, PLR, MPV and PDW of the groups were summarized in table 5. No statistically significant differences were observed between these groups with regard to NLR, LMR, RPR, PLR, MPV and PDW values ($p > 0.05$) (Table 6).

Discussion:

Complete blood count is a widely used laboratory test in clinical practice and includes white blood cell, red blood cell and platelet counts, and their morphological indices, such as MPV and RDW.

RDW measures the variability in the size of erythrocytes. An elevation in RDW levels shows immature red blood cell production in the bone marrow; thus, an increased RDW is often observed in patients with hematological diseases such as vitamin B12 or folate deficiency or hemolysis¹¹. Therefore, we excluded the anemic patients from the study. Also increased RDW occurs in patients with acute pancreatitis, colon cancer, infectious disease, septic shock and coronary artery disease^{5,6,8,10}. Theoretically, the relationship of RDW with these diseases may be due to its association with inflammation⁵. In chronic subclinical inflammation of cardiovascular events, increased RDW values, independently associated with higher levels of inflammatory markers such as C-reactive protein and interleukin-6, may associate with the adverse effect of disease on erythropoiesis by different mechanisms which may result in the release of immature RBCs into peripheral circulation¹². In recent studies, Chen et al. used the RPR to predict hepatic fibrosis stages in patients with chronic Hepatitis B to reduce the necessity for a liver biopsy for these patients whereas Cetinkaya et al. used RPR test to predict mortality in acute pancreatitis^{6,13}. Using this ratio may reflect the inflammation severity of these diseases. However, in our study, there was no statistically significant relation either between ISSHL patients and healthy individuals or in the prognosis of ISSHL. This situation may be due to the acute onset of the ISSHL.

Ommen et al.¹⁴ introduced a decrease in total and a relative number of circulating lymphocytes during acute myocardial infarction and advanced congestive heart failure. On account of this, the ratios of

neutrophils and platelets to lymphocytes are powerful markers of atherosclerotic disease with neutrophil and platelet indicating the systemic inflammatory status and severity of thrombosis¹⁵.

NLR is a widely available marker of inflammation that can classify the risk status of patients with various diseases^{16,17}. It is valuable as expensive inflammatory markers, such as IL-6, IL-1 β , IL-8, and TNF- α ¹⁸. In recent studies, the value of NLR has been also studied in the diagnosis and the prognosis of ISSHL¹⁹⁻²⁴. The higher levels of NLR in unrecovered patients of ISSHL was explained with the higher inflammation situation of these patients^{19,23}. Therefore, in these studies, NLR was suggested as a quick and reliable indicator for diagnosis and prognosis of ISSHL^{19-21,23}. PLR is also associated with atherosclerosis and inflammation of microvascular structures^{15,25}. Seo et.al. presented increased levels of NLR and PLR in recurrent and non-recurrent ISSHL and recommended to monitor these ratios at the clinic to predict recurrency of ISSHL²⁴. However, in another study, Seo et.al. could not find a relation between the PLR and the hearing recovery of the ISSHL²⁰. In our study, we showed that the NLR levels were significantly higher in ISSHL group than the control group. But we found no significant difference in response to treatment levels. We didn't find any statistically significant relation of PLR between the patient and control groups as well.

Monocytes play important roles in the inflammatory response, which is essential for the innate immune response to pathogens. Monocytes accompany in host defense against viral diseases through a variety of mechanisms, including phagocytosis of virus particles and virus-antibody complexes, augmentation of lymphocyte activities, and selective cytotoxicity for virus-infected cells²⁶. Seo et al. documented significantly different monocyte values between ISSHL patients and the control group²⁰. But they explained this difference by the theory of monocyte values could be increased due to

increased WBC value. In our study, we calculated the lymphocyte-to-monocyte ratio. This ratio in peripheral circulation may reflect the capacity of effective immune response of an individual. Our patient group has significantly different value of LMR from the control group while the comparison of the patients according to their hearing levels of hearings, there was no statistically significant difference.

MPV and PDW have easily measured platelet indices. They increased with the activation of the platelets²⁷. The relation of increased MPV level with the atherothrombosis has been assessed in the literature^{28,29}. The relationship of MPV and ISSHL was also previously assessed in a few studies, but the results were controversial^{19,30,31}. Ulu et al. compared MPV levels of ISSHL patients with healthy individuals and they found statistically significant difference between these two populations³¹. Ulu et al. also displayed significantly higher PDW levels in ISSHL. However, when Karli et al. and Kum et al. compared ISSHL patients with healthy individuals, they did not find any significant difference in MPV levels^{19,30}. The MPV analysis of our groups supported the results of Karli et al. and Kum et al. However, our PDW study showed up a significant difference between the patient and control groups. In addition, Mirvakili et al. showed a significant correlation between PDW and hearing loss severity of ISSHL patients³². In recent studies, the value of PDW is greater than platelet count and MPV to show the platelet activation²⁷. In our study, significance only in PDW values may be due to the PDW's being a more specific indicator of platelet activation.

Conclusion

NLR, MLR, and PDW values show the inflammatory status of ISSHL, but they do not indicate the prognosis. In this case, the availability of these parameters in monitoring the severity of the disease is controversial. Also, this is the first study investigating

the relation between ISSHL and LMR in the literature. Further prospective studies should be composed to shed light on the relation of ISSHL and LMR.

Compliance with Ethical Standards:

Financial disclosure: There is no funding or financial disclosure.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved by the research ethical committee of the Fatih Sultan Mehmet Education and Research Hospital in Istanbul, Turkey as a review (protocol number: 25.04.2016-485).

Informed consent: Routine informed consent was obtained from all patients before the hospitalization and also informed consent from the individuals of control group was obtained in the study.

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