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RESEARCH

HEMATOLOGIC PARAMETERS IN GERIATRIC PATIENTS WITH IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

ABSTRACT

Introduction: To assess the validity of complete blood count (CBC) parameters in the diagnosis and prognosis of idiopathic sudden sensorineural hearing loss (ISSNHL) in geriatric patients.

Material and Method: Sixty-two patients (women, 36; men, 26; mean age of all patients, 51±19 years) with ISSNHL were included in our study, and 49 healthy volunteers (women, 33; men, 16; mean age of all volunteers 48.6 ± 16.2 years) with no history of audiologic complaints or diseases formed the control group. Subjects in both the control and study groups were further divided into two groups according to their ages (<65 years and ≥65 years). CBC results were evaluated. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated.

Results: NLR and PLR values in patients diagnosed with sudden hearing loss were much higher compared to those in the control group. However, in geriatric patients, there was no difference in NLR and PLR between the study and control groups. There was also no difference in mean platelet volume (MPV) levels between the control and study groups at all ages. Red cell distribution width (RDW) was higher in both geriatric and non-geriatric patients with ISSNHL compared with the control group. When NLR, LPR, MPV, and RDW of patients with ISSNHL were compared between those who responded and those who did not respond to the standard treatment, there was no significant difference between the groups.

Conclusion: NLR, PLR, and RDW are increased in ISSNHL patients aged <65 years but only RDW is increased in geriatric patients with ISSNHL.

Key Words: Geriatrics; Hearing Loss, Sudden; Lymphocyte; Mean Platelet Volume; Neutrophils; Erythrocyte Indices.

ARAŞTIRMA

ANİ İDİOPATİK SENSORİNÖRAL İŞİTME KAYBI OLAN GERİATRİK HASTALARDA HEMATOLOJİK DEĞERLER

ÖZ

Giriş: Ani idiopatik sensorinöral işitme kaybı olan geriatrik hastaların tanı ve prognozunu değerlendirimede tam kan sayımı değişkenlerinin geçerliliğini belirlemek

Gereç ve Yöntem: Ani idiopatik sensorinöral işitme kaybı olan 62 hasta (36 kadın, 26 erkek; yaş ortalaması: 51±19) çalışma grubu ve tamamen sağlıklı, herhangi bir odyolojik şikayeti ve hastalığı olmayan 49 gönüllü (33 kadın, 16 erkek; yaş ortalaması: 48,6±16,2 yaş) kontrol grubunu oluşturmak üzere araştırmamıza katıldı. Çalışma ve kontrol grubunda yer alan katılımcılar yaş aralıklarına göre (<65 yaş ve ≥65 yaş olmak üzere) iki gruba daha ayrıldı. Tam kan sayımı sonuçları değerlendirildi. Nötrofil lenfosit oranı (NLR) ve Platelet lenfosit oranı (PLR) hesaplandı.

Bulgular: Çalışma grubundaki hastalarda kontrol grubuna oranla NLR ve PLR oranlarında belirgin bir artış gözlenmiştir. Ancak; geriatrik hastalarda NLR ve PLR sonuçlarında çalışma ve kontrol grubu sonuçlarında farklılık gözlenmemiştir. Ortalama platelet hacmi (MPV) seviyelerinde de kontrol ve çalışma grubu sonuçları bütün yaş gruplarında karşılaştırıldığında farklılık görülmemiştir. Kırmızı hücre dağılım genişliği (RDW) ise geriatrik ve geriatrik olmayan ani idiopatik işitme kayıplı hastalarda kontrol grubuna oranla yüksek bulunmuştur. Çalışma grubunda NLR, PLR, MPV ve RDW sonuçları tedaviye cevap veren ve vermeyen hastalarda karşılaştırıldığında faklılık bulunmadı.

Sonuç: NLR, PLR ve RDW değerleri ani idiopatik sensorinöral işitme kaybı olan <65 yaş olan hastalarda yüksek bulundu; ancak sadece RDW değeri ani idiopatik sensorinöral işitme kaybı olan geriatrik hastalarda yüksek bulundu.

Anahtar Sözcükler: Geriatri; İşitme Kaybı; Lenfosit; MPV; Nötrofil; RDW.

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Introduction

Sudden sensorineural hearing loss (SSNHL) is defined as sensorineural hearing loss of 30 decibels (dB) or more, over a minimum of 3 consecutive audiometric frequencies, occurring within a 72-hour period (1,2). It has been shown to affect 0.005%–0.02% of the population per year (3). SSNHL with no identifiable cause despite adequate investigations is termed idiopathic sudden sensorineural hearing loss (ISSNHL) (2).

Neutrophils, lymphocytes, and platelets are important blood cell elements. Platelets are crucial for coagulation, thrombosis, inflammation, and atherosclerosis (4). MPV (mean platelet volume) is a blood marker related to the function and activation of platelets (5) and is also a marker of atherosclerosis, suggesting that it is an important prophylactic and diagnostic tool in thrombotic and prothrombotic cases (6).

The red cell distribution width (RDW) is a routine laboratory parameter that indicates the variability in the size of circulating erythrocytes. The main area in which RDW is used is in the differential diagnosis of microcytic anemia. It has been defined as a prognostic tool in different clinical conditions, such as cardiovascular diseases and pulmonary artery hypertension (7). It has also been reported as an important predictor of mortality in the general population and older adults (8).

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been defined as novel markers of inflammation and thrombotic events, which can be easily measured from the complete blood count (CBC) (9). SSNHL, Bell's palsy, and vestibular neuritis are certain pathological conditions that have been found to be related to NLR and PLR in otolaryngological practice (10-12). However, some studies have confounding results about this issue (13).

In the literature, we did not come across any study delineating the correlation between inflammatory and thrombotic parameters of CBC such as NLR, PLR, MPV, and RDW with the diagnosis and prognosis of ISSNHL in geriatrics. For this reason, we grouped ISSNHL patients and healthy volunteers according to their ages (<65 years old and >65 years old) and compared their CBC results.

Materials and Method

The present study was approved by the Institutional Review Board of the Ufuk University Medical School with decision number 30042015-7. All patients signed informed consent forms before participating in the study.

Patient Selection

Patients with a decrease in hearing ≥30 dB, affecting at least 3 consecutive frequencies within a 72-hour period or less, were considered as having SSNHL. Patients having vestibular schwannoma, stroke, malignancy, recent acoustic trauma, history of migraine, severe head trauma, usage of ototoxic medications, type 1 or 2 diabetes mellitus, hypertension, renal failure, or vertigo at the beginning of the disease were excluded from study. Patients with fluctuating hearing loss, isolated low frequency hearing loss were also excluded from study.

These patients and age- and sex-matched healthy volunteers were then divided into two groups according to their ages. Patients and healthy volunteers aged ≥65 years old formed the geriatric group while participants aged <65 years old formed the non-geriatric group.

Subjects were divided into four groups according to their ages: Group 1 comprised patients with ISSNHL aged <65 years old (36 patients; mean age 37.1±11.8 years); Group 2 comprised patients with ISSNHL aged ≥65 years (26 patients; mean age 70.2±5.8 years); Group 3 comprised healthy volunteers <65 years (32 patients; mean age 38.2±8.7 years); and Group 4 comprised healthy volunteers ≥65 years (17 patients; mean age 68.3±2.5 years). Groups 1 and 2 formed the study groups, while groups 3 and 4 formed the control groups.

All study participants underwent the tests outlined below.

Laboratory Measurements

Blood samples for biochemical parameters were taken after a minimum of an 8-hour overnight fast. CBC parameters of the blood samples were simultaneously measured and analyzed with a hematology analyzer (CELL-DYN Ruby Hematology System, Illinois, USA). Hemoglobin, erythrocyte, leukocyte, neutrophil, lymphocyte, RDW, platelet counts, and MPV results of all the participants were evaluated by obtaining the samples of all patients included in the study before the treatment. Subsequently, NLR (neutrophil-to-lymphocyte ratio) and PLR (platelet-to-lymphocyte ratios) values were calculated.

Audiological Examination

After middle ear pathologies were excluded by otologic examination and tympanometry (AZ 26 Clinical Audiometer; Interacoustics, Assens, Denmark), pure tone audiometry was performed (AC 33 Clinical Audiometer; Interacoustics, Assens, Denmark) in a totally isolated cabin between 250–8000 Hz frequencies. Pure tone average (PTA) was established as the simple arithmetic mean for frequencies of 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz. The speech

discrimination scores (SDS) were also obtained. SDS measured by 50 selected monosyllabic words at an easily detectable hearing level and the percentage of words correctly identified was calculated.

Hearing thresholds were noted at the onset of treatment and in the second week and the sixth month of treatment. Improvement of hearing (recovery) was defined as return to within 10 dB of the unaffected ear or >10dB improvement in PTA or 15% recovery in SDS. "No recovery" was defined as <10 dB improvement in PTA (2).

Pretreatment audiograms were categorized into four sensorineural types: upsloping, downsloping (falling curve), mid-frequency (flat or U-shaped curve), and profound loss (a flat audiogram with a threshold shift >90 dB in all frequencies). The upsloping (raising) curve was not included in this study because patients with upsloping curves also had vertigo at onset of ISSNHL.

Treatment Strategy

Oral prednisone (1 mg/kg; maximum dose 60 mg/day) in a single dose for 14 days was administered as the initial therapy for patients with ISSNHL[2]. Hyperbaric oxygen therapy was offered to patients with ISSNHL if there was no response to treatment within 3 months.

Statistical Analysis

The analysis of the results was performed using IBM SPSS Statistics (Armonk, New York, USA) version 21.0 software for Windows. Data were tested for normal distribution using the Kolmogorov–Smirnov test. To investigate the differences between groups, Mann–Whitney U test was used for two groups and Kruskal–Wallis H test for >2 groups. Chi-square test was performed for categorical variables. Post-hoc comparisons with Conover's multiple comparison test was used. Statistical significance was defined as $p<0.05$.

Results

Subjects

After 18 patients were excluded (3 patients had vertigo at the onset of hearing loss, 2 had a history of previous sudden hearing loss, 2 had bilateral sudden hearing loss, 6 had diabetes mellitus, and 5 had atherosclerotic vascular disease), 62 patients [36 (58.1%) women; mean age of all patients 51±19.0 years (range: 21–83 years)] were included in this study. Forty-nine healthy volunteers [33 (67.3%) women; mean age of all volunteers 48.6±16.2 years (min–max: 26–72 years)] who had no history of audiologic complaints or diseases formed the control group. There was no significant difference between the study and control groups in terms of gender and age ($p=0.32$ and $p=0.52$, respectively).

The demographics of the study and control groups are shown in Table 1.

Table 1— Demographics, Hemogram, Plasma Lipid Profiles, C-reactive Protein (CRP), Erythrocyte Sedimentation Rates (ESR), NLR, and PLR Values of the Study and Control Groups.

	Study Group [mean(sd)] (n=62)	Control Group [mean(sd)] (n=49)	p
Gender M/F (Female %)	26/36 (58.1 %)	16/33 (67.3 %)	0.32
Age	51 (19)	49 (16.2)	0.519
Cholesterol (mg/dL)	198 (46.6)	193.3 (46.6)	0.601
LDL (mg/dL)	120.4 (36)	116.6 (35.6)	0.585
HDL (mg/dL)	45.3 (11.7)	48.8 (11.2)	0.115
TG (mg/dL)	139.2 (79)	117.5 (59)	0.103
CRP (mg/dL)	3 (3.3)	3.1 (3.3)	0.820
ESR	2 (1.1)	2.3 (1.3)	0.267
Hb (g/dL)	14 (1.6)	14.3 (1.6)	0.389
White Blood Cell (10^3/µL)	7.2 (1.4)	7 (1)	0.127
Neutrophil (10^3/µL)	5 (1.8)	4 (1.5)	0.002
Lymphocyte (10^3/µL)	2 (0.8)	2.1 (0.6)	0.298
Platelet (10^3K/ µL)	234 (53.5)	236 (39)	0.840
Mean Platelet Volume (fL)	8.1 (1.2)	8.4 (1.2)	0.172
RDW (%)	13.4 (1.8)	14.7 (2.2)	0.001
NLR	3.1 (2.4)	2 (0.8)	0.002
PLR (10^3)	143 (83)	118 (31.2)	0.032

(LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; Hb: Hemoglobin; CRP: C-reactive protein; RDW: Red cell distribution width)

Table 2— NLR and PLR Values of Young Patients (<65 years old) in the Study (Group 1) and Control (Group 3) Groups.

	Group 1 [mean(sd)] (n=36)	Group 3 [mean(sd)] (n=32)	p
Gender M/F (Female %)	16/20 (55.6 %)	9/23 (71.9 %)	0.164
Age	37 (11.8)	38.2 (8.7)	0.635
Cholesterol (mg/dL)	190.7 (46.9)	189 (45.9)	0.880
LDL (mg/dL)	117.3 (36.3)	111.1 (35.4)	0.479
HDL (mg/dL)	44.2 (11.4)	51.7 (12)	0.222
TG (mg/dL)	136.5 (89.2)	110.3 (55.5)	0.157
CRP (mg/dL)	2.9 (3.8)	3.4 (3.9)	0.561
ESR	1.9 (1)	2.3 (1.3)	0.161
Hb (g/dL)	14.2 (1.9)	14.2 (1.6)	0.962
White Blood Cell (10^3/μL)	7.4 (1.4)	6.7 (0.7)	0.001
Neutrophil (10^3/μL)	5.2 (1.9)	3.8 (0.8)	< 0.001
Lymphocyte (10^3/μL)	1.9 (0.8)	2 (0.5)	0.954
Platelet (10^3K/ μL)	241 (56)	238 (33)	0.829
Mean Platelet Volume (fL)	7.9 (1.3)	8.3 (1.2)	0.162
RDW (%)	13.5 (2.03)	14.6 (2.2)	0.04
NLR	3.3 (2.8)	2.7 (2.2)	0.010
PLR (10^3)	149 (63)	137 (64)	0.042

(LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; Hb: Hemoglobin; CRP: C-reactive protein; RDW: Red cell distribution width)

Audiologic Test Results

Audiologic test results in terms of PTA and SDS in control and study groups before treatment are shown in Table 2. In the study groups, 35 (56.5%) patients had ISSNHL in the left ear and 27 (43.5%) in the right ear. Pretreatment audiogram types in the study groups were as follows: type 1 (upsloping) in 4 (6.5%) patients; type 2 (downsloping) in 10 (16.1%) patients; type 3 (U shaped) in 38 (61.3%) patients; and type 4 (profound loss) in 10 (16.1%) patients. There was no statistically significant difference between the study and control groups with respect to the side affected and type of audiograms (p=0.50 and p=0.13, respectively).

Laboratory Measurement Results

Hemogram, plasma lipid profiles, C-reactive protein (CRP), erythrocyte sedimentation rates (ESR), RDW, MPV, NLR, and PLR values and demographics are shown in Table 1, 2 and 3. In young patients, NLR, PLR and RDW significantly differed between ISSNHL and control groups (Table 2) while only RDW was significantly higher in ISSNHL group in elderly patients (Table 3).

Treatment Response Results

In the study groups (Groups 1 and 2), 26 (41.9%) patients were responsive to oral steroid treatment, and 7 (19.4%) of 36 patients who were unresponsive to oral steroids were responsive to hyperbaric oxygen treatment. Thus, in the study groups, 29 patients (46.8%) were unresponsive to treatment, while 33 (53.2%) patients were responsive to treatment. In addition, response and non-response to oral steroid therapy was evaluated among the two age groups of ISSNHL patients. In Group 2 (elderly group), 10 (38.5%) patients were responsive to oral steroid treatment, while 16 (61.5%) patients were not responsive. In Group 1, 44% of patients were responsive to oral steroid therapy, while 56% were unresponsive. When ages of patients with ISSNHL were compared between those responsive and unresponsive to both oral steroid and hyperbaric oxygen treatments, no significant difference was found between groups (p=0.14).

Treatment response did not change based on the side of the ear with hearing loss (p=0.85). However, there was a relationship between the audiogram type and response to treatment; 68.4% of patients with U-shaped audiograms were responsive to treatment, but no patient with profound hearing loss was responsive to treatment (p=0.001).

Table 3— NLR and PLR Values of Elderly Patients in the Study (Group 2) and Control (Group 4) Groups

	Group 2 [mean(sd)] (n=26)	Group 4 [mean(sd)] (n=17)	p
Gender M/F (Female %)	16/10 (61.5 %)	10/7 (58.8 %)	0.565
Age	70 (5.8)	68.3 (2.5)	0.923
Cholesterol (mg/dL)	208 (41.9)	201.5 (48.1)	0.969
LDL (mg/dL)	124.7 (35.8)	127.1 (34.7)	0.996
HDL (mg/dL)	47 (12.1)	43.4 (7.2)	0.750
TG (mg/dL)	144.1 (63.5)	130.8 (64.6)	0.932
CRP (mg/dL)	3.1 (2.5)	2.6 (1.4)	0.950
ESR	2.2 (1.1)	2.2 (1.3)	0.981
Hb (g/dL)	13.8 (1.3)	14.4 (1.4)	0.577
White Blood Cell (10^3/µL)	6.8 (1.4)	7.4 (1.2)	0.404
Neutrophil (10^3/µL)	4.5 (1.6)	4.4 (2.2)	0.997
Lymphocyte (10^3/µL)	2 (0.8)	2.3 (0.5)	0.341
Platelet (10^3 K/ µL)	224 (49)	230 (49)	0.976
Mean Platelet Volume (fL)	8.2 (1.2)	8.4 (1.2)	0.960
RDW (%)	15 (2.4)	13.2 (1.5)	0.015
NLR	2.7 (1.8)	2 (1)	0.562
PLR (10^3)	134 (84)	103 (28)	0.409

(LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride; Hb: Hemoglobin; CRP: C-reactive protein; RDW: Red cell distribution width)

When NLR, LPR, MPV, and RDW of patients with ISSNHL were compared between the patients responsive and unresponsive to both oral steroid and hyperbaric oxygen treatments, no significant difference was found between groups (p=0.96; p=0.22; p=0.45; p=0.98, respectively).

Discussion

The major finding of this prospective clinical study is that in geriatric ISSNHL patients, only RDW values were increased and were significantly different from those of healthy volunteers. NLR and PLR values did not differ between the geriatric populations of both the control group and ISSNHL patients. Moreover, none of the parameters including NLR, PLR, MPV, and RDW predicted the prognosis of the disease in geriatric patients.

The etiopathogenesis of ISSNHL is not yet clearly understood, although many theories including infections, blood disorders, vascular pathologies, immune disorders, ototoxic drugs, and metabolic conditions have been reported to explain the pathophysiology of ISSNHL (14). Therefore, both inflammatory and thrombotic markers are being investigated to explain the cause of ISSNHL and to plan treatment strategy.

NLR is an easily available and inexpensive method of diagnosing inflammatory diseases in geriatric patients. A recent study in which 43 patients over 65 years of age were recruited revealed higher NLR values that were related with acute appendicitis (15). In addition, in 242 geriatric patients with type 2 diabetes, Ozturk et al. showed that increased NLR values were associated with microvascular complications (16). A larger study with 507 patients has shown that geriatric patients with coronary artery disease have higher NLR values (17). There are many studies pertaining to ISSNHL disease in non-geriatric patients showing that NLR values were significantly higher in sensorineural hearing loss than in the control group. Similarly, mean NLR was higher in non-responsive patients when compared with responsive patients. A significant correlation was observed between NLR values and the severity of hearing loss, indicating the presence of inflammation (7,13).

Similarly, PLR is also an inflammatory marker that is inexpensive to study. NLR and PLR are among the laboratory markers introduced into clinical practice for the purpose of evaluating systemic and subclinical inflammation (18). Previous studies showed that in various diseases, PLR value could be used as an inflammatory marker and correlated with poor prognosis (19). Besides cardiovascular diseases, the studies about ISSNHL showed similar findings (20). However, some authors believe there is not enough evidence and that

these results may be affected by other patient comorbidities and the inflammatory process of the disease (14). However, there was no study in the literature about PLR in geriatric patients.

MPV reflects the size of platelets and can be used as a marker for high platelet activity, which plays an active role in the pathophysiology of thrombosis, coagulation, and atherosclerosis. Previous studies have controversial results about MPV values in ISSNHL patients. The studies conducted by Karlı et al. (5) and Kum et al. (7) found no significant difference in MPV between the study and control groups in contrast to the findings of Ulu et al. (21) and Sagit et al. (22). However, no study has been reported concerning MPV in geriatric patients as yet.

To our knowledge, our study is the first study in the literature which assessed NLR, PLR, and MPV in geriatric ISSNHL patients. In this study, we did not find any difference in NLR, PLR, and MPV in geriatric patients with ISSNHL. These findings could have been affected by the exclusion of patients with comorbidities, such as diabetes mellitus and hypertension, which could influence the results. In addition, we found higher NLR and PLR values in the study group than in the control group in the younger population in this study, and this was similar to the results of some other manuscripts in the literature (12,13). This difference between young and old patients in NLR and PLR values may be explained by the increased incidence of atherosclerosis in elderly patients without any known disease. As asymptomatic atherosclerosis may also change the inflammatory parameters, the increase in these parameters in ISSNHL group may be masked by the presence of asymptomatic atherosclerosis in the control group. Another explanation to our findings may be the altered inflammatory response of the elderly patients to different conditions, i.e. ISSNHL in our study.

In the current study, we did not find relationship between NLR, PLR, MPV values and treatment response, and we assume that the cause of this finding could be the small sample size of our study.

Increased RDW values have been reported to be related with underlying chronic inflammation which promotes red blood cell membrane deformability and changes in erythropoiesis (23). However, RDW can be considered as a dynamic variable with rapid changes associated with acute disease states, such as acute myocardial infarction and acute decompensated heart failure (24). Wen et al. believe that RDW is associated with the presence of carotid plaque and carotid intima–media thickness (IMT) and is therefore related with stroke (25). In the literature, only Yasan et al. studied RDW in ISSNHL; they did not find any difference between the study and control groups. It must be noted that the control group of the study included patients with indication for septoplasty, and hence, the RDW results of the control group may not represent healthy individuals. In this study, higher RDW levels were observed in ISSNHL patients than in controls for all ages. The singular parameter which could be used in the diagnosis of ISSNHL in geriatric patients was RDW. The mechanism of the association between increased RDW and ISSNHL is unclear; however, some theories, such as inflammatory and thrombotic processes, causing impaired erythropoiesis could be postulated. However, studies about the relationship between SSNHL and RDW must be conducted to precisely determine the mechanisms involved.

There are several limitations of the study. First of all, the sample size of the study was small because it was a single-center study. In addition, it was a prospective study conducted over a relatively short period. Besides, other parameters related with inflammatory and thrombotic involvement may be studied to explore the significant findings; however, studying these parameters may increase incur higher expenses.

In conclusion, we investigated CBC parameters in the diagnosis and prognosis of geriatric ISSNHL patients in the current study. The single parameter of CBC count affected in geriatric patients was RDW, and the other parameters, including NLR, PLR, and MPV, should not be used for diagnosis in geriatric ISSNHL patients.

Conflict of Interest

All authors have no conflict of interest to declare.

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