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Is there any relationship between hematologic parameters and presbycusis in geriatric patients?

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Abstract

Aim: Presbycusis is the most common sensory deficit in the aging population. Blood examinations are inexpensive and simple methods for analyzing red cells, white cells and platelets for coagulation, inflammation, thrombosis. In the present study, we aimed to investigate the relationship between presbycusis and inflammatory and prothrombotic factors that can be measured routinely in complete blood count (CBC) tests with little cost in addition with hearing loss types.

Material and methods: The study was conducted prospectively. Group I comprised patients with presbycusis aged ≥65 years (n=31), group 2 was constituted by healthy volunteers aged ≥65 years (n=30). Audiograms were categorized according to hearing levels at 0.5, 1, 2, 4, and 8 kHz: high-frequency steeply sloping (HFSS), flat configuration, high-frequency gently sloping (HFGS). Complete blood counts including hemoglobin (Hb), RDW (red cell distribution width), WBC (white blood cell), neutrophil-to-lymphocyte ratio (NLR), platelets (PLT), platelet-to-lymphocyte ratio (PLR), PCT(procalcitonin), PDW (platelet distribution width), MPV (mean platelet volume), and fibrinogen were analyzed.

Results: There were no significant differences between the patient and control groups in terms of Hb, RDW, WBC, NLR, PLT, PCT, PDW, MPV, PLR and fibrinogen ($p>0.05$). There were no significant differences between the FLAT, HFSS and normal groups in terms of mean Hb, RDW, WBC, NLR, PLT, PCT, PDW, MPV, PLR and fibrinogen ($p>0.05$).

Conclusion: No difference was detected in terms of the presbyacusis, hearing loss types and CBC parameters. According to the study results presbyacusis types and inflammatory mediators did not correlate with each other.

Keywords: presbycusis, geriatric, complete blood count, inflammatory markers, hearing loss

ГЕРИАТРИЯЛЫҚ ПАЦИЕНТТЕРДЕ ГЕМАТОЛОГИЯЛЫҚ ПАРАМЕТРЛЕР МЕН ЕСТУ ҚАБІЛЕТІН ЖАС ҰЛҒАЮЫНА БАЙЛАНЫСТЫ ЖОҒАЛТУ АРАСЫНДА АРАҚАТЫНАС БАР МА?

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ТҰЖЫРЫМДАМА

Мақсаты: Пресбиакузис (есту қабілетін жас ұлғаюына байланысты жоғалту) – бұл қартаюшы адамдар арасындағы ең көп таралған сенсорлық бұзылу болып табылады. Қан зерттеуі - бұл эритроциттерді, лейкоциттерді және тромбоциттерді қан ұюына, қабынуға және тромбозға талдаудың арзан және қарапайым тәсілі. Осы зерттеудің мақсаты пресбиакузис пен протромботикалық факторлардың арақатынасын зерттеу болып табылады, олар есту қабілетін жоғалту типіне қосымша қан талдауынан айқындалуы мүмкін.

Әдістері: Бұл зерттеу проспективті, оның қатысушылары екі топқа бөлінді. 1 топқа ≥65 жас (n=31) шамасындағы пресбиакузиспен ауыратын пациенттер кірді, 2-топқа ≥65 жас (n=30) шамасындағы дені сау еріктілер кірді. Аудиограммалар 0.5, 1, 2, 4, және 8 кГц есту деңгейіне сәйкес санаттар бойынша бөлінді: қатты көлбеу жоғары жиілікті, тегіс конфигурация, жеңіл көлбеу жоғары жиілікті. Гемоглобинді, эритроциттер көлемін үйлестіру енін, лейкоциттерді, нейтрофилдер мен лимфоциттердің қатынасы индексін, тромбоциттерді, тромбоциттер мен лимфоциттердің қатынасын, прокальцитонинді, тромбоциттерді үйлестіру енін, тромбоциттердің орташа көлемін және фибриногенді қамтитын қанға жалпы талдау жасалынды.

Нәтижелері: Гемоглобинге, эритроциттер көлемін үйлестіру еніне, лейкоциттерге, нейтрофилдер мен лимфоциттердің қатынасы индексіне, тромбоциттерге, тромбоциттер мен лимфоциттердің қанытасына, прокальцитонинге, тромбоциттерді үйлестіру еніне, тромбоциттердің орташа көлеміне және фибриногенге ($p>0.05$) қатысты пациенттер мен бақылау тобы арасында айтарлықтай айырмашылық айқындалған жоқ. Есту қабілеті қатты көлбеу тегіс конфигурациялы және жоғары жиілікті конфигурациялы пациенттер мен сау топ арасында сол гематологиялық параметрлерге қатысты айтарлықтай ерекшелік айқындалған жоқ.

Қорытынды: Пресбиакузис, есту қабілетін жоғалту типі және қанның жалпы талдауының параметрлеріне қатысты ерекшеліктер айқындалған жоқ. Зерттеу нәтижелеріне сәйкес пресбиакузис типтері мен қабыну медиаторлары бір-бірімен байланысты емес.
Негізгі сөздер: пресбиакузис, гериатриялық пациент, қан талдауы, қабыну маркерлері, есту қабілетін жоғалту

ЕСТЬ ЛИ ВЗАИМООТНОШЕНИЕ МЕЖДУ ГЕМАТОЛОГИЧЕСКИМИ ПАРАМЕТРАМИ И ВОЗРАСТНОЙ ПОТЕРЕЙ СЛУХА У ГЕРИАТРИЧЕСКИХ ПАЦИЕНТОВ?

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РЕЗЮМЕ

Цель: Пресбиакузис (возрастная потеря слуха) – это наиболее распространенное сенсорное нарушение среди стареющего населения. Исследования крови являются недорогими и простыми методами анализа эритроцитов, лейкоцитов и тромбоцитов на свертываемость, воспаление и тромбоз. Целью настоящего исследования является изучение взаимоотношения между пресбиакузисом и протромботическими факторами, которые могут быть регулярно определены из общего анализа крови с незначительными затратами в дополнение к типу потери слуха.

Материал и методы: Настоящее исследование проспективное, участники которого были разделены на две группы. В группу 1 вошли пациенты с пресбиакузисом в возрасте ≥65 лет (n=31), в группу 2 вошли здоровые добровольцы в возрасте ≥65 лет (n=30). Аудиограммы были распределены по категориям в соответствии с уровнем слуха 0.5, 1, 2, 4, и 8 кГц: высокочастотная с сильным наклоном, плоская конфигурация, высокочастотная с легким наклоном. Проведен общий анализ крови, включающий гемоглобин, ширину распределения объёма эритроцитов, лейкоциты, индекс соотношения нейтрофилов и лимфоцитов, тромбоциты, соотношение тромбоцитов и лимфоцитов, прокальцитонин, ширину распределения тромбоцитов, средний объем тромбоцитов, и фибриноген.

Результаты: Значительной разницы между пациентами и контрольной группой в отношении гемоглобина, ширины распределения объёма эритроцитов, лейкоцитов, индекса соотношения нейтрофилов и лимфоцитов, тромбоцитов, соотношения тромбоцитов и лимфоцитов, прокальцитонина, ширины распределения тромбоцитов, среднего объема тромбоцитов, и фибриногена (p>0.05) не обнаружено. Значительной разницы между пациентами с уровнем слуха плоской конфигурации и высокочастотной конфигурации с сильным наклоном и здоровой группы в отношении тех же гематологических параметров не обнаружено.

Заключение: Не обнаружено различий в отношении пресбиакузиса, типом потери слуха и параметрами общего анализа крови. В соответствии с результатами исследования, типы пресбиакузиса и медиаторы воспаления не связаны друг с другом.

Ключевые слова: пресбиакузис, гериатрический пациент, общий анализ крови, маркеры воспаления, потеря слуха

Introduction

Age-related hearing loss, also known as presbycusis (PC), is characterized by bilateral sensorineural hearing loss, slowed central processing of acoustic information, and speech perception difficulties in noisy environments. PC is the most common sensory deficit in the aging population and is associated with a diminished quality of life [1]. It has been shown to affect 500 million people in 1.2 billion over 60 years in 2025 according to the World Health Organization [2]. Hearing aids are typically used for rehabilitation. The causes of presbycusis has been focused on hereditary factors and other preventable factors such as noise exposure, exposure to ototoxic medication or chemicals, cardiovascular risk factors, diabetes, smoking, and chronic middle ear diseases. Recent findings have changed the understanding of the pathophysiology of PC and have forced a reconsideration of the sequence of events by which hearing loss in the elderly develops. Besides hearing aids, early detection and prevention of PC may be the most successful therapeutic strategy [3].

Blood examinations are inexpensive and simple methods for analyzing red cells, white cells and platelets. It is about coagulation, inflammation, thrombosis. Routine blood data include hemoglobin content (Hb), red cell distribution width (RDW), white blood cell (WBC), platelets (PLT), mean platelet volume (MPV), procalcitonin (PCT), and platelet distribution width (PDW). In addition, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) can be calculated. Some of these are markers of inflammation, some are for atherothrombosis and may promote a prothrombotic or hypercoagulable state [4].

In this study, we aimed to investigate the relationship between presbycusis and inflammatory and prothrombotic factors that can be measured routinely in complete blood count (CBC) tests with little cost. We found no studies delineating these parameters with presbycusis and comparing these results.

Material and methods

The present study was conducted in the Department of Otorhinolaryngology and Head and Neck Surgery of our clinic. Our study was approved by the local ethics committee (2018/341) and conducted in accordance with the ethical principles described by the Declaration of Helsinki. Informed consent was obtained from all participants before the study. The study was conducted prospectively and the study group (group I) included 31 patients who were diagnosed as having presbycusis in November and December 2018. The control group (group II) comprised 30 age-matched healthy subjects who were aged over 65 years and were asymptomatic with unremarkable medical histories and normal physical examinations. Patients with isolated low frequency hearing loss, chronic otitis media, otosclerosis, a history of acoustic trauma, Meniere's disease, vertigo, and prior ear surgery were excluded from the study. Regarding co-morbid diseases, patients with acute infection, malignancy, using ototoxic medications, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, renal-liver-pulmonary diseases were also excluded. Group I comprised patients with presbycusis aged ≥65 years (n=31), group 2 was constituted by healthy volunteers aged ≥65 years (n=30). The audiologic and biochemical-hematologic data of the study participants were investigated.

Auditory evaluation

The ear, nose, and throat examinations were completed before the audiometric tests. The patient's ears were evaluated and otoscopic views were normal detected. Pure tone audiometry was performed between 250-8000 Hz frequencies using the PC-based Clinical Audiometry/Otometrics Madsen Astrera. A qualified audiologist performed the testing. Audiometric patterns were assessed. Speech discrimination scores (SDS) were also obtained. The Turkish version of monosyllabic phonetically balanced word lists were used for evaluating the SDS. Audiograms were categorized according to hearing levels

at 0.5, 1, 2, 4, and 8 kHz: high-frequency steeply sloping (HFSS), flat configuration, high-frequency gently sloping (HFGS). The difference between the mean of 500 Hz/1 kHz thresholds and the mean of 4 kHz/8 kHz thresholds is greater than 30 Db in HFSS, and between 15-29 dB in HFGS. The difference between the mean of 250/500 Hz thresholds, the mean of 1/2 kHz thresholds and the mean of 4/8 kHz thresholds is less than 15 dB in flat presbycusis [5].

Biochemical and hematologic analysis

Blood samples were collected after a fasting period of approximately 12 hours. Complete blood counts including hemoglobin, RDW, WBC, platelets, PCT, PDW, MPV, and fibrinogen were analyzed using an XN-1000 (Sysmex) Hematology Analyzer. The NLR was calculated as the ratio of neutrophils to lymphocytes and PLR was calculated as the ratio of platelets to lymphocytes. Mean values were used for statistical analysis.

Statistical analysis

The SPSS 21 package program was used in data analyses. Normal distribution of the data was checked using the Shapiro-Wilk test. Hb, RDW, WBC, NLR, PLT, PCT, PDW, MPV, PLR and fibrinogen variables were normally distributed. Student's t-test was used to compare the means between the patient and study groups and one-way analysis of variance (ANOVA) was used to compare the means between the FLAT, HFSS, and normal groups. The HFGS group consisted of one patient who was not included in the analyses. Descriptive statistics are expressed as mean, standard deviation, minimum and maximum values. The homogeneity of sex distribution in the patient and control groups was controlled using the Chi-square test. Descriptive statistics are expressed as frequency and percentage. The level of statistical significance was taken as 0.05 for all analyses.

Results

There was no difference between the groups in terms of mean age (p=0.857). The mean age was 75.55±8.41 years in the patient group and 75.20±6.51 in the control group. Sex distribution in the groups was homogeneous (F/M: 16/15 in the patient group and 15/15 in the control group) (p=0.9). The audiometric configuration of the patients was as follows: 20 (32.8%) patients with flat type, 10 (16.4%) with HFSS, and 1 (1.6%) with HFGS.

There were no significant differences between the patient and control groups in terms of Hb, RDW, WBC, NLR, PLT, PCT, PDW, MPV, PLR and fibrinogen(p>0.05) (Table 1).

There were no significant differences between the FLAT, HFSS and normal groups in terms of mean Hb, RDW, WBC, NLR, PLT, PCT, PDW, MPV, PLR and fibrinogen (p>0.05) (Table 2).

Table 1 Mean values of hematologic parameters of group 1 and 2.

	Group I		Group II		
	Mean±SD	Min-Max	Mean±SD	Min-Max	P
Hb	13.25±0.94	11.90-15.00	13.69±1.01	11.30-16.10	0.078
RDW	13.96±1.01	12.50-16.00	13.71±1.06	12.50-17.30	0.341
WBC	7.17±1.83	4.00-10.10	6.96±1.61	4.66-10.80	0.634
NLR	1.93±0.79	0.39-3.91	2.01±0.75	0.90-3.60	0.686
PLT	254.42±56.00	150.00-400.00	253.17±51.70	188.00-400.00	0.928
PCT	0.23±0.06	0.13-0.37	0.23±0.05	0.15-0.35	0.627
PDW	14.84±2.92	9.60-18.40	14.65±1.75	11.90-17.80	0.762
MPV	9.22±1.16	6.79-11.80	9.19±1.77	6.50-13.40	0.946
PLR	123.95±46.02	67.15-215.00	133.27±41.42	61.50-215.00	0.409
FIBRINOGEN	320.83±59.54	212.00-399.00	328.04±64.35	210.00-420.00	0.651

p: Student's t-test

Table 2 Distribution of laboratory data according to audiometric configuration

	FLAT		HFSS		NORMAL		
	Mean±SD	Min-Max	Mean±SD	Min-Max	Mean±SD	Min-Max	p
Hb	13.05±0.84	11.90-14.70	13.57±1.10	12.00-15.00	13.69±1.01	11.30-16.10	0.072
RDW	14.03±0.98	12.50-16.00	13.90±1.13	12.70-15.90	13.71±1.06	12.50-17.30	0.559
WBC	7.10±1.83	4.00-10.00	7.02±1.77	4.05-9.75	6.96±1.61	4.66-10.80	0.961
NLR	2.11±0.83	1.00-3.91	1.56±0.63	0.39-2.40	2.01±0.75	0.90-3.60	0.166
PLT	255.10±63.25	150.00-400.00	247.90±40.82	184.00-312.00	253.17±51.70	188.00-400.00	0.943
PCT	0.23±0.06	0.13-0.37	0.23±0.05	0.15-0.28	0.23±0.05	0.15-0.35	0.886
PDW	15.49±2.42	10.80-17.70	14.07±3.42	9.60-18.40	14.65±1.75	11.90-17.80	0.247
MPV	9.22±1.23	7.20-11.80	9.23±1.12	6.79-10.40	9.19±1.77	6.50-13.40	0.997
PLR	134.16±50.45	68.10-215.00	106.47±31.89	67.15-170.70	133.27±41.42	61.50-215.00	0.204
FIBRINOGEN	311.15±64.94	212.00-398.00	334.97±46.71	270.00-399.00	328.04±64.35	210.00-420.00	0.528

p: One-way ANOVA

Discussion

Recently, many studies have shown that routine blood parameters can be used to diagnose sudden hearing loss and to predict its prognosis. Unfortunately, we could not find any studies that have explored the relationships between presbycusis, its subgroups, and routine blood parameters. This study was designed to investigate whether inflammatory markers in CBC and fibrinogen played a role in the etiology of presbycusis by comparing the hematologic parameters of patients with presbycusis aged over 65 years and individuals with normal hearing levels. There was no significant difference between the patient and control groups in terms of inflammatory marker values. We divided hearing loss into HFSS, HFGS, and flat types, considering that different regions of the cochlea might have different sensitivity to inflammatory processes, and we examined the blood values of each type, separately. The HFGS group consisted of one patient who was not included in the analyses. We found no relation between different hearing loss types and inflammatory markers.

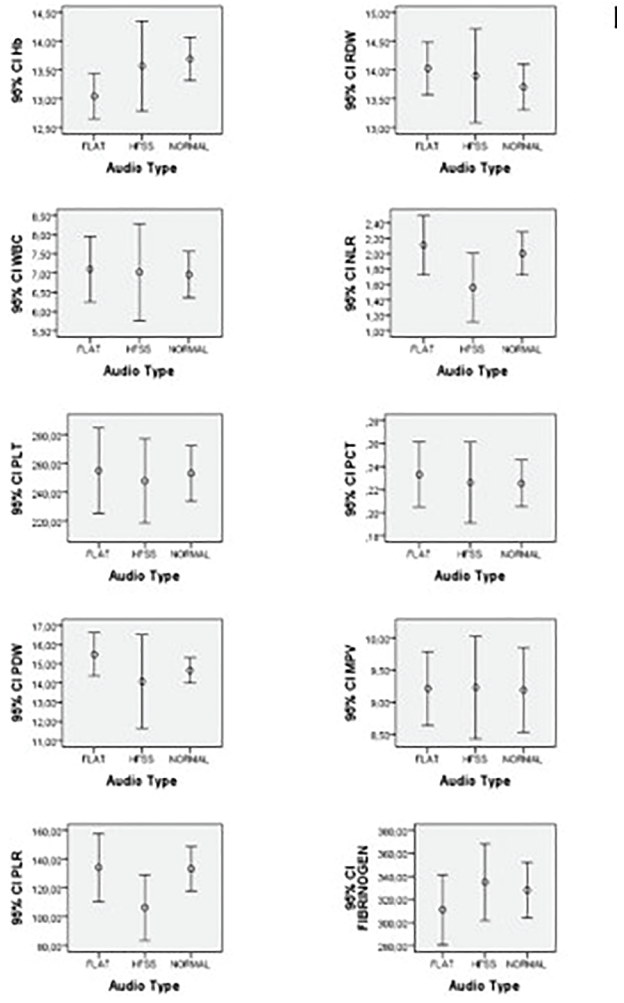

Figure 1 - Mean values of Hb, RDW, WBC, platelet, NLR, PLT, PDW, PCT and fibrinogen according to audio types.

The effects of chronic inflammation on the cochlea were evaluated by Watson et al. in their study of presbycusis, and they showed that aging could cause chronic inflammation in the cochlea as well as in many tissues in their literature scan. However, it was observed that markers used to evaluate chronic inflammation such as tumor necrosis factor (TNF) alpha, interleukin (IL)-6, IL-1 beta and C-reactive protein (CRP) were expensive in that study [6]. In our study, we used inexpensive and widely available markers. The inflammation process is an immunosenescence phenomenon, including normal fluctuations caused by an aging immune system. This age-related immunosenescence process, as a result, causes the body to become increasingly worse in controlling or reducing the production of pro-inflammatory proteins during and after immune responses. As a result, there is an increasing inflammatory state in many aging tissues [7].

There are studies investigating the effects of chronic inflammation on cardiovascular disease, type II diabetes , and Alzheimer's disease. Naturally, the cochlea may also be affected by this process. The accumulation of pro-inflammatory cytokines and reactive molecules designed to target pathogens in cells eventually damages the body's own tissue structure [8]. If this damage occurs in the inner ear, it is inevitable that the hearing will be affected. Then, could exposure of an inner ear to sound, even it is not high intensity, for at least 65 years cause local chronic inflammation? Could accumulation of pro-inflammatory proteins due to aging of the immune system without the presence of a chronic disease cause hearing loss? And, could blood laboratory tests show this chronic inflammation? The relationship between presbycusis and inflammation is not a frequently investigated subject. Vershcuur et al. concluded that inflammation was part of the mechanisms underlying presbycusis [9]. The Aspirin in reducing events in the elderly (ASPREE-Hearing) study was performed by the only group to investigate inflammation in presbycusis. The group is examining the potential therapeutic benefits of low-dose aspirin, a weak anti-inflammatory agent, in PC. The aim of the study is to determine whether this basic treatment can reduce the progression of the disease in older individuals. This large-scale clinical study being performed in Australia includes 1262 people aged 70 years and over and is still ongoing. The results have not been published yet [10].

Schucnect and Gacek divided presbycusis into 6 groups. These were sensory, neural, metabolic or striatal, cochlear conductive, mixed, and indeterminate types. Presbycusis types are then paired with audiometric patterns. HFSS is seen with sensory type, flat type is seen with striatal type, and HFGS is seen with cochlear type. Flat type-striatal presbycusis is the most common. Inheritance is very important in striatal type. The second most common is sensory type-HFSS and exposure to noise and chemical pollutants is common in this type [5]. In our study, the most common type was flat type and the second most common was HFSS. HFGS was detected in one patient who was not included in the statistical analyses. Neuronal type, which is associated with a significant decrease in speech, was not found among our patients. Blood tests were performed in all patients but no significant relation was found between the type of audiograms and the blood test values.

As age progresses, proinflammatory cytokines such as IL-6 and TNF alpha are increased, erythrocyte maturation is affected, glycoprotein production, iron metabolism, RBC lifespan and erythropoietin sensitivity change. In chronic inflammation, RDW is increased due to changes in red blood cell membrane deformability and erythropoiesis. However, elevated RDW is also detected in dynamic conditions such as acute myocardial infarction (MI), heart failure, and stroke [11, 12]. Yasan et al. found no relation between acute-onset hearing loss and RDW [13]. However, Ezerarslan et al. showed that RDW was increased in acute-onset hearing loss in all age groups [14]. We did not include patients with such acute pathologies in our study. In fact, RDW has a high correlation with inflammatory markers; it does not correlate with age, sex, and hematologic variations [15]. In our study, we found no difference between patients with presbycusis

and controls in terms of RDW and hemoglobin levels. WBC and subtypes are accepted as classic inflammatory markers. NLR can be easily obtained by dividing the neutrophil numbers by the lymphocyte numbers. These inflammatory markers are relatively inexpensive and easy to obtain compared with IL6, IL-1 beta, and TNF alpha. NLR is a safe marker to use in all diseases such as cardiovascular diseases, Alzheimer's disease, ulcerative colitis, and appendicitis, where inflammation plays a role in the pathogenesis. Tuhanioglu et al. found no difference in NLR and MPV between patients with mild-moderate OSAS and severe OSAS in patients aged both above and below 65 years [16]. NLR, which is used to show endothelial dysfunction and inflammation, increases in high frequency hearing loss in patients with diabetes in whom endothelial dysfunction plays a role [17]. NLR is studied mostly in the pathogenesis of sudden-onset hearing loss. It was found that NLR increased in patients with acute onset hearing loss and also in patients whose hearing loss did not improve, which suggests that inflammation is occurring [18]. There was no significant difference between our NLR values in two groups.

Platelets play an active role in thrombosis, coagulation, inflammation, and atherosclerosis. MPV is a marker of platelet size and reactivity, showing increased prothrombotic state and hypercoagulability as its value increases because large platelets are enzymatically and metabolically more active [19]. There are studies showing that MPV is an important marker in inflammatory diseases such as rheumatoid arthritis. Sagit et al. showed that MPV increased in acute-onset hearing loss [20]. PLR is used to assess the extent of systemic inflammation and reflects endothelial damage in the peripheral vascular system. Increased PLR shows increased platelet adhesion to newly damaged vessels [21]. Increased MPV and PLR in acute hearing loss in high frequencies and increased MPV in all frequencies are related with poor prognosis [22]. We found no difference between the study and control groups in terms of MPV and PLR in our study.

PCT is a prototype of a “hormokine” mediator that is released in bacterial infections, but not in viral infections or non-infectious stimuli [23]. We found no change in PCT levels in our study. PDW is an inflammatory marker that can increase in inflammatory conditions and malignancies [24]. Fibrinogen is an acute phase protein that is part of the coagulation cascade and is converted into the insoluble protein fibrin during the clotting process. It has a clinical impact on the occurrence and outcome of various diseases, such as coagulopathies, or ischemic stroke and also obstetrical complications [25]. The prognosis of acute hearing loss was investigated in a study and it was found that individuals affected by up-sloping hearing loss had better prognosis and only fibrinogen levels affected prognosis [26]. In our study, however, we observed no changes in fibrinogen levels.

Conclusion

MPV, PLR, RDW, NLR, PDW, and fibrinogen are inexpensive and easy-to-use markers in the evaluation of inflammation. This is the first study in the literature to investigate the relation between these markers in patients with presbycusis. Although these markers are useful and inexpensive, they are not affected in presbycusis. Also, they are not affected in different audiometric types of presbycusis, means the equable sensitivity in different affected areas in cochlea. This may be due to the small sample size in our study, which may decrease the statistical power. Further, this was a prospective study conducted over a relatively short period. We need to expand the number of patients with presbycusis and follow them for longer periods in further studies.

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