NKMJ
Namık Kemal Tıp Dergisi
Namık Kemal Medical Journal

Research Article /Araştırma Makalesi
Doi: https://doi.org/10.37696/nkmj.656479 e-ISSN: 2587-0262

MEAN PLATELET VOLUME TO LYMPHOCYTE RATIO: A NOVEL MARKER FOR IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

Ortalama Trombosit Hacminin Lenfosit Sayısına Oranı: İdiopatik Ani Sensörinöral İşitme Kaybında Yeni Bir Belirteç

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The study was conducted in accordance with the ethical principles described by the Declaration of Helsinki and the approval was obtained from Gaziosmanpaşa University Ethics Committee for Clinical Investigations (Approval number:18-KAEK-266).

Abstract

Aim: To investigate the value of mean platelet volume (MPV) to lymphocyte ratio (MPVLR), a novel marker, in determining the prognosis of sudden sensorineural hearing loss (SSNHL).

Materials and Methods: This retrospective cross-sectional study study included the patient group consisting of 65 SSNHL and the control group consisting of 50 healthy individuals. 65 patients with SSNHL were divided into two subgroups as 44 recovered patients and 21 unrecovered patients. The SSHNL patients and the control group, and the recovered SSNHL patients and the unrecovered SSNHL patients were compared statistically in terms of MPV, lymphocyte count and MPVLR.

Results: The mean MPV value was 9.28 ± 0.99 fL in the patients and 9.25 ±0.82 fL in the control group, and the difference was not statistically significant (p = 0,851). The mean lymphocyte count was 1.90 ± 1.02 in the study group and 2.55± 0.78 in the control group, and the difference was statistically significant (p <0.001). The mean MPVLR value was 6.44 ± 4.14 in the study group and 4.03 ± 1.62 in the control group and the difference was statistically significant (p<0,05).

Conclusion: MPVLR is an easily accessible marker and levels are increased by severity of the disease. The lymphocyte count is also declined according to the severity of the disease. These results showed that MPVLR and lymphocyte count can help to predict the SSNHL prognosis. With future studies, the value of MPVLR in the prognosis of SSNHL may be better understood.

Keywords: Mean platelet volume to lymphocyte ratio; mean platelet volume; sudden sensorineural hearing loss.

Öz

Amaç: Yeni bir marker olan MPVLR (Mean platelet volume to lymphocyte ratio) nin SSNHL (Ani sensörinöral işitme kaybı)' nin prognozunda kullanılabilirliğini araştırmak.

Materyal ve Metot: Bu retrospektif kesitsel çalışma 65 SSNHL li hasta ile 50 sağlıklı bireyden oluşan kontrol grubunu içermektedir. SSNHL li 65 hasta tedaviye cevap veren.44 hasta ile tedaviye cevap vermeyen 21 hasta olarak ikiye ayrılmıştır. SSNHL li hastalar ile kontrol grubu ve tedaviye cevap veren SSNHL'li hastalar ile tedaviye cevap vermeyen SSNHL li hastalar MPV (Mean platelet volume), lenfosit miktarı ve MPVLR açısından istatistiksel olarak karşılaştırılmıştır.

Bulgular: Ortalama MPV değeri hastalarda 9.28 ± 0.99 fL iken çalışma grubunda 9.25 ±0.82 fL idi ve istatistiksel olarak farklı değildi (p = 0,851). Ortalama lenfosit miktarı çalışma grubunda 1.90 ± 1.02 iken kontrol grubunda 2.55± 0.78 idi ve istatistiksel olarak farklıydı (p <0.001). Ortalama MPVLR değeri çalışma grubunda 6.44 ± 4.14 iken kontrol grubunda 4.03 ± 1.62 idi ve istatistiksel olarak farklıydı (p<0,05).

Sonuç: MPVLR kolay ulaşılabilen ve hastalığın şiddetine göre düzeyi artan bir belirteçtir. Lenfosit sayısı da hastalığın düzeyine göre düşmektedir. Bu sonuçlar MPVLR ve lenfosit miktarının SSNHL nin prognozunu belirlemede yardımcı olabileceğini göstermektedir. Gelecekteki çalışmalar SSNHL'nin prognozunu belirlemede MPVLR değerinin daha iyi anlaşılmasını sağlayabilir.

Anahtar Kelimeler: Ortalama trombosit hacmi: lenfosit oranı; Ortalama trombosit hacmi; ani sensörinöral işitme kaybı.

INTRODUCTION

Idiopathic sudden sensorineural hearing loss (SSNHL) is a situation characterized by sensorineural hearing loss of more than 30 dB in three consecutive frequencies in pure tone audiometry over the

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Article History / Makale Geçmişi:

Date Received / Geliş Tarihi: 06.12.2019
Date Accepted / Kabul Tarihi: 29.04.2020

past three days. The incidence varies between 5-20 and 160 in 100000 cases[1]. While men and women are equally affected, the mean age at disease onset is between 43 and 53. Between 25% and 53% of patients can have ear fullness, tinnitus and vertigo[2]. It is thought that many factors are responsible for the etiology of SSNHL, such as viral causes, chronic inflammation, immunological diseases and microvascular circulatory disorders. However, the causes in the majority of cases are unknown[1,3]. The time to start treatment, type of audiogram, presence of vertigo, degree of hearing loss, age and gender has been used to determine the prognosis of SSNHL [4].

Mean Platelet Volume (MPV) is a parameter that shows the size of platelets, and that is routinely encountered in complete blood count (CBC) and easily accessible. Since large platelets are an indicator of increased aggregation and increased adhesion molecules, high MPV levels are indicative of platelet reactivation[5].

Mean Platelet Volume to lymphocyte ratio (MPVLR) was first defined by Hudzik et al. as a new marker. They reported a correlation between the increased mortality of the patients with ST elevation cardiac myocardial infarction and the significantly increased MPVLR, levels [6]. The relationship between MPV and SSNHL were also reported in many studies [3,7]. But, the present study is the first study that adressed the MPVLR as a prognostic marker in SSNHL as far as we know. The aim of this study is to investigate the value of MPVLR, a new marker, in determining the prognosis of SSNHL.

MATERIALS AND METHODS

This study was designed as a retrospective, cross-sectional cohort study and consisted of the SSNHL patients and the healthy control group.

Patient Selection

The study group consisted of 65 patients who were admitted with SSNHL to the Tokat State Hospital Otorhinolaryngology Department between January 2013 and January 2019. All of the patients had no previous history of smoking or otologic diseases (chronic otitis media, otosclerosis, acoustic trauma history, Meniere's disease, vestibular schwannoma etc.). Patients with systemic disorders (diabetes mellitus, hypertension, autoimmune or chronic inflammatory disease), chronic lung diseases, acute or chronic cardiac diseases, obstructive sleep apnea syndrome were excluded from the study. The patients were evaluated with pure tone audiometry, blood tests and temporal bone magnetic resonance imaging with gadolinium contrast (MRI) after the routine otoscopic examination. The control group was conducted with 50 healthy individuals without any abnormalities in routine blood tests, had normal audiogram results and normal temporal bone MRI.

All of the patients with SSNHL were treated routinely with metil-prednisolone therapy (1 mg / kg / day p.o) and therapy was terminated in 2 weeks with gradual dose reduction [8].

Patient follow-up

Siegel criteria were used to evaluate the hearing levels of patients before and after treatment (Table 1) [9]. The recovered subgroup (complete + partial + slight) the unrecovered subgroup (no improvement) consited of 44 and 21 patients, respectively.The audiological evaluation was made to all patients at first admission and one month later controls.

Table 1. Siegel criteria (9)

Type	Evaluation	Explanation
1	Complete recovery	Final hearing level is 25 dB or better, regardless of the amount of gain
2	Partial recovery	More than 15 Db gain and final hearing is between 25-45 dB
3	Poor recovery	More than 15 db hearing gain and final Hearing is 45 db or worse
4	No recovery	Gain less than 15 dB

Sample Collection

Blood samples were obtained from all subjects during the initial application. The mean value of MPV (Normal value: 6.5–11.6 fL) and lymphocyte count (Normal value: 1.09–2.99 10^3 /uL) was determined using the fully automatic blood cell counter (BC-6800, Mindray®, Guangdong, China). MPVLR was calculated by dividing the mean value of MPV by the count of lymphocytes. Mean values obtained from blood tests were used in statistical analysis.

Audiometry

All of the participants were underwent otoscopic examination before the audiological assessments and examined with pure tone audiometer. Air and bone conduction levels were analyzed at 0.5, 1, 2, 4 kHz frequencies, all examinations were performed using a calibrated clinical audiometer (AC 40 Interacoustics®, Assens, Denmark). Sudden sensorineural hearing loss was accepted as the sensorineural hearing loss that occurred in the last three days and were more than 30 dB in three consecutive frequencies in the audiometric evaluation.

Statistical Analysis

Statistical analysis were performed using SPSS software (v. 22.0, IBM®, Chicago, IL). All of the parameters were expressed as mean ± standard deviation. The Kolmogorov-Smirnov test was used to determine whether the parameters had normal distribution. Age, gender and laboratory parameters were evaluated in all groups and mean values were used in statistical analysis. MPV, MPVLR values and lymphocyte count were compared between patient, control group and subgroups. Student-t test was used to compare parameters with normal distribution, and Mann-Whitney U test was used to compare parameters with no normal distribution. $p<0.05$ value was considered statistical significant.

Ethical statement

The study was conducted in accordance with the ethical principles described by the Declaration of Helsinki and the approval was obtained from Gaziosmanpaşa University Ethics Committee for Clinical Investigations (Approval number:18-KAEK-266). All of the participants gave their decent consent before the study.

RESULTS

The mean age of the patient and control groups were 46.82 ± 12.91 and 47.36 ± 12.45 years, respectively. No statistical difference was found between the two groups in terms of age and gender.

The mean value of MPV was 9.28 ± 0.99 fL in the patients and 9.25 ±0.82 fL in the control group, and the difference was not statistically significant ($p = 0.851$). The mean lymphocyte value was 1.90 ± 1.02 10^3/uL in the study group and 2.55± 0.78 10^3/uL in the control group, and the difference was

statistically significant (p <0.001) (Table 2). The mean MPVLR value was 6.44 ± 4.14 in the study group and 4.03 ± 1.62 in the control group and the difference was statistically significant (p <0.001) (Table 2) (Figure 1).

Table 2. Statistical data between the study and control groups

	Sudden hearing loss(n=65)				*p*	Control (n=50)			
	Mean	**SD**	**Median**	**Q1-Q3**		**Mean**	**SD**	**Median**	**Q1-Q3**
MPV	9,28	0,99	9,10	8,8 - 9,90	0.851*	9,25	0,82	9,10	8,75 - 9,60
Lym.	1,90	1,02	1,88	1,2 - 2,20	<0.001**	2,55	0,78	2,50	2,025 -2,99
MPVLR	6,44	4,14	5,17	3,90 - 7,83	<0.001**	4,03	1,62	3,55	3,04 - 4,70

** Student t test*, *** Mann Whitney U test*
Abbrevations: MPV: Mean platelet volume, MPVLR: Mean platelet volume to lymphocyte ratio, Lym: Lymphocytes

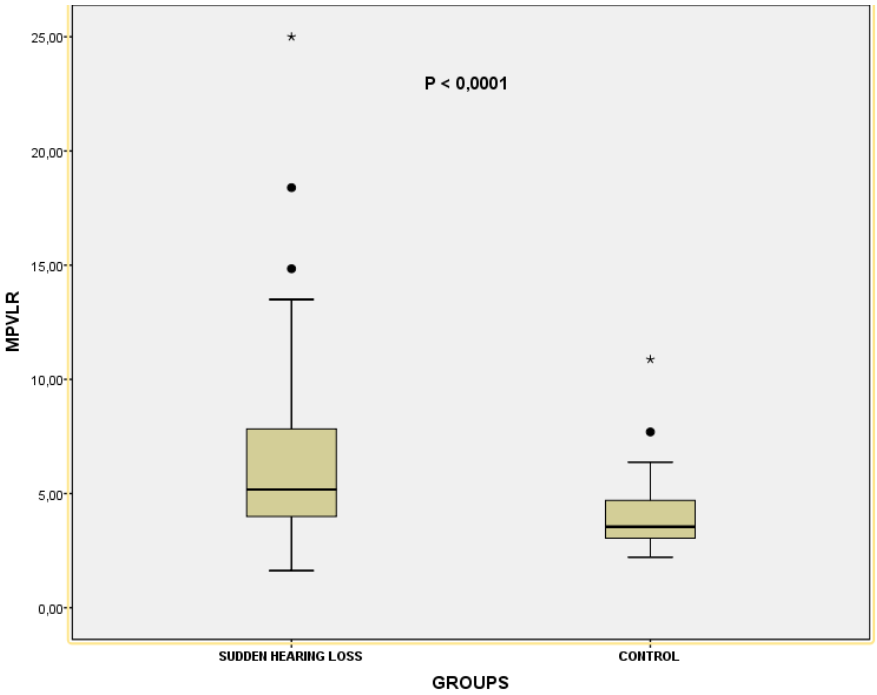

Figure 1. MPVLR ratios between study and control groups p<0.05.

The mean value of MPV of the recovered subgroup was 9.14 ± 0.90 and the mean value of MPV was 9.53 ± 1.11 in the unrecovered subgroup without any significant difference. The mean lymphocyte count was 2.17 ± 1.13 in the recovered subgroup and 1.45 ± 0.57 in the unrecovered subgroup, and the difference in terms of lymphocyte values was statistically significant (p =0.0103) (Table 3). The mean MPVLR value was 5.37 ± 2.97 in the recovered subgroup and 8.22 ± 5.19 in the unrecovered subgroup and the difference in terms of MPVLR values was statistically significant (p <0.001) (Table 3) (Figure 2).

Table 3. Statistical data between the treatment recovered and unrecovered groups.

	Sudden hearing loss								
	Recovered Group (n=44)				*p*	Unrecovered Group (n=21)			
	Mean	**SD**	**Median**	**Q1-Q3**		**Mean**	**SD**	**Median**	**Q1-Q3**
MPV	9,14	0,90	9,10	8,7 - 9,50	0,146*	9,53	1,11	9,55	8,9 - 10,3
Lymphocytes	2,17	1,13	1,90	1,4 - 2,60	0,0103**	1,45	0,57	1,30	1,00 - 2,00
MPVLR	5,37	2,97	4,79	3,44 - 6,90	0,0058**	8,22	5,19	6,16	4,68 - 9,70

** Student t test*, *** Mann Whitney U test*
Abbrevations: MPV: Mean platelet volume, MPVLR: Mean platelet volume to lymphocyte ratio

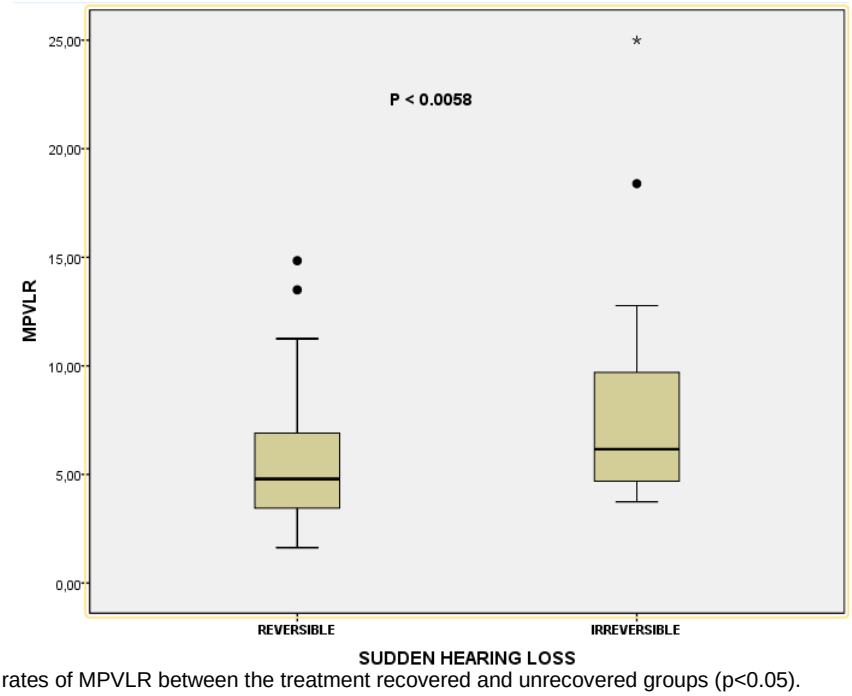

Figure 2. The rates of MPVLR between the treatment recovered and unrecovered groups (p<0.05).

DISCUSSION

In recent literature, different factors were blamed in the etiology of SSNHL that includes microcirculatory disorders, viral causes, immunologic factors and inflammatory causes for SSNHL but the precise cause was a still a dilemma [10,11]. The blood supply of the cochlea was provided by only the labyrinthine artery and this delicate arterial structure might be sensitive for circulatory disorder [12,13].

Previous studies were examined, it is seen that the increased rates of SSNHL in cardiovascular and thromboembolic events support the vascular occlusion hypothesis in the etiology of SSNHL. Besides that, diabetes mellitus and hypercholesterolemia are diseases that trigger atherosclerosis in large vessels, cerebral vessels and peripheral vessels[14]. In a prospective study performed with 35 SSNHL patients by Ullrich et al., they found that SSNHL increases in cases where cardiovascular risk factors such as obesity and hyperlipidemia increase[15]. In a study performed with 99 patients by Ballesteros et al., they found an association between SSNHL and cardiovascular risk factors[16].

Platelets are the cells that have a role in the formation of hemostasis and thrombosis in blood vessels. The mediators and substances secreted by platelets play an important role in coagulation, inflammation and thrombus formation and atherosclerosis. MPV is a parameter that shows the volume, activity and function of platelets. It was shown that MPV levels increase in atherosclerosis, acute syndromes, venous and arterial thrombosis [17]. In a study of Ulu et al., they compared the patients with SSNHL and the control group consisting of the same number of healthy individuals as the patients with SSNHL and they found significantly increased MPV values in the patients with SSNHL compared to the control group [18]. In contrast, Karli et al. asserted that MPV had no predictive value in patients with SSNHL [7]. Likewise, the results of our study also show that MPV is not a predictive value in SSNHL.

MPVLR was first investigated by Hudzik et al. in terms of its predictive value in the investigation of long-term mortality risk after myocardial infarction [6]. In a study of Hudzik et al., they asserted that MPVLR could be a predictive marker of early and late mortality in ST elevation myocardial infarction [6].

Kurtul et al. also found that the increased MPVLR value in ST-elevation myocardial infarction were correlated with early mortality [19]. Microangiopathy is a pathological condition seen in patients with SSNHL [20]. It is also known that there is a relationship between different cardiovascular pathologies and SSNHL [21]. In a case-controlled study, it was found that the incidence of SSNHL was higher in individuals of families with cardiovascular events compared to the individuals of families with no cardiovascular events [22].

In our study, while the MPVLR values were found to be increased in patients with SSNHL compared to the control group, and significantly increased in patients of unrecovered subgroup. Difference in MPV values were not significant in SSNHL patients. In the study of Durmus et al., they found that MPV values were significantly higher in the SSNHL unrecovered patients compared to the recovered group [3]. Similarly, Ulu et al. found that MPV was significantly higher in the patients with SSNHL, and they supported the idea that this situation in SSNHL was occurred by the effect of vascular insufficiency, ischemia and thrombosis [18]. In our study, the main cause of the increased MPVLR in the unrecovered group was not the fact that MPV value was high in the unrecovered group, but the mean lymphocyte value was low.

Lymphocytes are cells that play an important role in inflammatory response. The lymphocytes count that was decreased by the induced apoptosis may increase inflammatory damage [23]. Kassner et al suggested the proadhesive and proinflammatory cytokines such as CD38 and CD40 may lead the lymphocyte extravasation. As a result of the related blood cell's transmigration, blood cell counts may be decreased for a certain of time [24]. In our study, we also found the decreased number of lymphocytes in SSNHL group and the decline of lymphocyte cell count was more significant in unrecovered group. This results may support the inflammatory process hypothesis and we speculate this result with lymphocyte count may help to predict the SSNHL prognosis.

Our study includes some limitations. These are the retrospective nature of study and the cohort consisting of patients with relatively small number. However, the present study is the first study investigating the relationship between MPVLR and SSNHL in literature as far as we know.

CONCLUSION

MPVLR is an easily calculated marker. In SSNHL, the MPVLR level increased by severity of the disease shows that it can be a marker for prognosis in this disease. With future studies, the value of MPVLR in the prognosis of SSNHL may be better understood.

Conflict of interest: None

Funding: None

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