RESEARCH ARTICLE
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Are Platelet Distribution and Volume Values Parameters for Meniere's Disease?

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ABSTRACT

Objective: To evaluate the relationship between mean platelet volume (MPV), platelet distribution width (PDW), as well as the other parameters of complete blood counts (CBC) and diagnosis and prognosis in Meniere's disease (MD).
Material and Methods: Complete blood count data of 54 MD patients who were followed in our clinic between 2010 and 2018 and age/sex-matched controls were analyzed retrospectively. MPV, PDW, and the other parameters of CBC were compared. Subjects with normal serum glucose, cholesterol, vitamin, and liver and kidney function test levels were included in the study. Subjects with chronic diseases that may affect CBC values were excluded. The Meniere's group was divided into subgroups according to the degree of hearing loss and CBC values were compared within subgroups.
Results: MPV and PDW values were significantly high in the Meniere's group. There was no significant difference in the other parameters of CBC between the MD and control groups. Statistically significant correlation was obtained in MPV and PDW values in the Meniere's group. As the audiometry values increased, MPV and PDW were found to increase.
Conclusion: MPV and PDW, which are markers of vascular pathology, might be potential new serum markers in Meniere's disease.

Keywords: Complete Blood Counts; Meniere's Disease, Mean platelet volume, Platelet distribution width, Sensorineural hearing loss

INTRODUCTION

Meniere's Disease (MD) is defined as an idiopathic syndrome characterized by recurrent episodes of vertigo, hearing loss, fullness in the ear, tinnitus, and endolymphatic hydrops in the inner ear (1). The hearing loss in MD is of the sensorineural type and is initially in fluctuant style, which holds low frequencies (200-600Hz) (2). As the course of MD progresses, the hearing level decreases at other frequencies and flat hearing loss occurs (3).

Although many factors are suspected in the etiology of MD, the exact cause is still unclear (4). Endolymphatic hydrops has been the most important finding in studies on the pathophysiology of MD (5). Endolymphatic hydrops is associated with endolymph release, absorption dysfunction, and endolymphatic duct obstruction (6). Factors such as genetic predisposition, autoimmune disease, inflammation, endocrine system abnormalities, viral infections, vascular system abnormalities, allergy, syphilis, leukemia, and trauma are at fault in the hydrops mechanism.

Vascular mechanisms of MD have been attributed to decreased intracerebral arterial pressure, venous obstruction, chronic CSF pressure increase, and chronic hypoxia, which reduce the perfusion rate (7). It has been reported that disruption of the venous absorption mechanism of endolymph as a result of these mechanisms may be associated with vascular pathology (5, 8, 9). The vascular pathology that disrupts this hemostasis

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balance in MD is the presence of venous insufficiency in the paravestibular canalicular (PVC) vein network, which is very important for the inner ear fluid mechanisms (10).

Platelets involved in hemostasis play a role in the formation of thrombosis. Platelets secrete mediators that are important for coagulation, thrombosis, atherosclerosis, and inflammation (11). MPV shows the function and activity of platelets. Volumetrically large platelets are more metabolically and enzymatically active and have greater thrombotic potential (11). Mean platelet volume (MPV) is a marker used in systemic inflammatory conditions and cardiovascular pathologies (12). Platelet distribution width (PDW) represents heterogeneity in platelet morphology. MPV and PDW values are more specific parameters than platelet count in evaluating platelet function (12). MPV and PDW are complete blood count elements that can be performed quickly and cheaply in routine blood tests.

The amount of MPV and PDW is closely related to cardiovascular risk factor such as atherosclerosis, acute syndromes, venous and arterial thrombosis, carotid and peripheral artery disease, or thromboembolism (13-15). In the study by Ulu et al., MPV value was found to be significantly higher in patients with sudden hearing loss and it was associated with vascular pathologies (16). Likewise, in the study by Sagit et al., MPV and PDW values were found to be significantly higher in patients with sudden hearing loss (17).

In the present study, we aimed to evaluate MPV and PDW, as well as the other parameters of complete blood counts (CBC), supporting the hypothesis of vascular pathology in MH. To the best of our knowledge, this is the first study to evaluate CBC parameters in MD.

MATERIALS AND METHODS

Ethics committee approval was obtained from the Local Ethics Committee (Ethics Committee No:71522473/050.01.04/162). The study was carried out by retrospectively examining the records of patients diagnosed with MD who applied to the ENT clinic of Sakarya University Training and Research Hospital.

Fifty-four patients who presented with peripheral vertigo attack and were diagnosed with MD after detailed anamnesis, physical examination and tests were included in the study. Routine blood test results and audiometry values of these patients during the attack period and at the 3rd month after the attack were evaluated. Patients were evaluated with respect to CBC, glucose, cholesterol, liver function tests, renal function tests, and vitamin B9 and B12. Audiometric and vestibular tests (VHIT, VNG) were performed to differentiate peripheral and central vertigo. It was requested that patients who had not been diagnosed with neurological diseases be evaluated for them. At the end of this process, patients diagnosed with MD were included in the study. The control group was selected from the patients who applied to the otorhinolaryngology outpatient clinic for routine checkups. Patients in the control group who were found to have pathology (such as vertigo, nasal septum deviation, nasal polyposis, sensory hearing loss, obstructive sleep apnea syndrome, malignancy) in the detailed otolaryngology examination were excluded from the study. People with any chronic disease were not included in either group so that the CBC value was not affected.

Neutrophil, lymphocyte, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) MPV, and PDW values were compared. Glucose, cholesterol, liver function tests, renal function tests, and vitamin values were evaluated in both groups, in order to avoid any chronic disease that might affect CBC values.

The affected ear was identified in the Meniere's group. Meniere's patients were divided into subgroups according to the degree of hearing loss on the affected ear side during the non-attack periods and during the attack periods. Hearing losses were found to be 0-25 dB normal hearing, 26-40dB mild sensorineural hearing loss (SNHL), 41-70dB medium SNHL, 71-90dB advanced SNHL, and 91dB + profound SNHL, according to the pure sound averages of 500, 1000, 2000, and 4000Hz.

Statistical Analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) 22.0 program. Hematological data were analyzed by the Shapiro-Wilk test for normal distribution in each group and subgroups. Descriptive results of the data with normal distribution according to normality distribution were stated as mean±SD, and non-normal distribution was defined as median [IR]. The normal distribution data of the groups were compared with the independent-samples t-test and the non-normal distribution data were compared with the Mann-Whitney U test. The normal distribution of CBC data of subgroups according to hearing loss in the Meniere's group were compared with the one way ANOVA test, and the non-normal distribution data were compared with the Kruskal Wallis test. MPV and PDW results which were statistically significant for these groups were evaluated by linear regression test. Results were evaluated at 95% confidence interval and $p<0.05$ significance level.

RESULTS

The mean age was 48.15±11.91 years and consisted of 26 (48.1%) women and 28 (51.9%) men in the Meniere's group. The mean age was 45.05±7.72 years and consisted of 25 (46.3%) women and 29 (53.7%) men in the control group. There was no significant difference between Meniere's and control groups in terms of age, sex, glucose, cholesterol, liver function tests, renal function tests, and vitamin values ($p\geq0.05$) (Table 1).

While there was no significant difference in neutrophil, lymphocyte, platelet, NLR, and PLR values between the Meniere's group and the control group in CBC ($p\geq0.05$), a statistically significant difference was found in MPV and PDW values ($p<0.05$) (Table 2) (Figure 1, Figure 2).

In the Meniere's group, 22 (40.7%) right and 32 (59.3%) left ears were affected. Meniere's patients during the attack period of the affected ears had 12 (22.2%) normal, 13 (24.1%) mild

Table 1: Glucose, cholesterol, renal and liver function tests and B12, folic acid mean values between control and Meniere's groups.

Variable	Meniere's group	Control group	p value
Glucose (mg/d)	100 [18.7]	99.5 [17]	0.411
Total cholesterol (mg/d)	198.7±26.1	199.3±44.8	0.217
HDL-cholesterol (mg/d)	49.9±11.4	45.7±9.9	0.879
LDL-cholesterol (mg/d)	124.5±26.8	129.4±35.7	0.758
AST (U/L)	22.5 [7]	18.0 [7]	0.462
ALT (U/L)	22.5 [13]	21.0 [15]	0.809
Serum urea (mg/dL)	29.2±7.2	28.6±8.4	0.374
Creatinine (mg/dL)	0.7 [0.16]	0.7 [0.15]	0.279
Vitamin B12 (pg/mL)	357 [124.7]	344 [181.7]	0.815
Folate (ng/mL)	7.0±2.3	6.46±2.2	0.816

Continuous variables were presented as mean ± standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein

Table 2: Mean values of neutrophils, lymphocytes, platelets, NLR, PLR, MPV, PDW between Meniere's and control groups.

Variable	Meniere's group	Control group	p value
Neutrophil count (10^9/L)	3.9 [1.7]	3.9 [2.3]	0.982
Lymphocyte count (10^9/L)	2.1 [1.2]	2.5 [0.9]	0.490
Platelet count (10^3/mm^3)	253.6±53.5	261.0±61.4	0.537
MPV (fl)	**7.98 [1.81]**	**7.53 [1.18]**	**0.023***
PDW (fl)	**18.2 ±1.1**	**17.5 ±0.6**	**0.001***
NLR	1.68 [1.12]	1.60 [1.11]	0.372
PLR	106.50 [48.50]	106.32 [53.79]	0.949

Continuous variables were presented as mean ± standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
*A statistically significant difference was obtained between MPV and PDW values.
MPV: Mean Platelet Volume, PDW: Platelet Distribution Width, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio

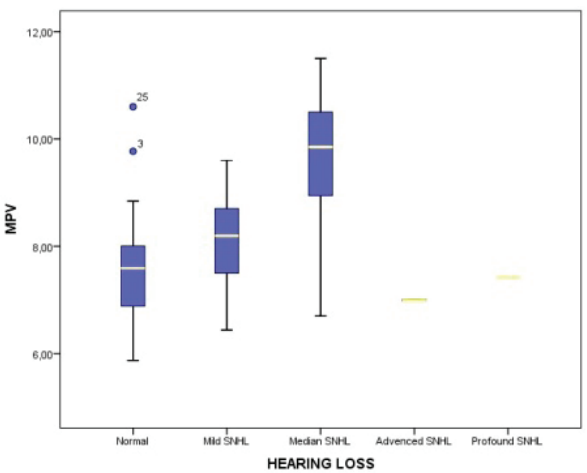

Figure 1: Distribution of MPV value between groups.

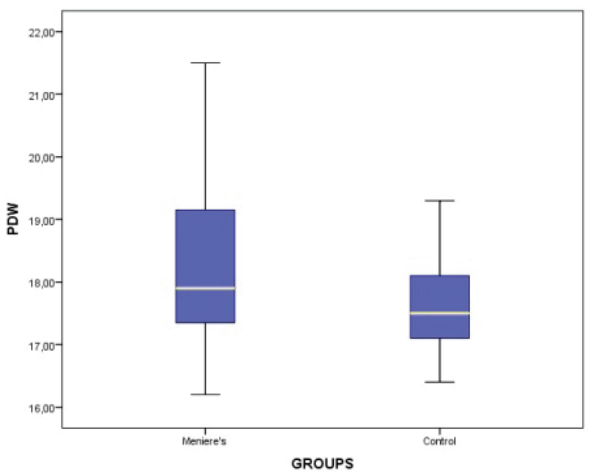

Figure 2: Distribution of PDW value between groups.

SNHL, 25 (46.3%) medium SNHL, 2 (3.7%) advanced SNHL, and 2 (3.7%) profound SNHL according to the pure sound averages of 500, 1000, 2000, and 4000Hz. There were no significant difference in CBC values according to the degree of hearing loss (p≥0.05) (Table 3).

During the nonattack period, 20 (37.1%) of Meniere's patients had normal hearing, 19 (35.1%) mild SNHL, 12 (22.2%) medium SNHL, and 2 (3.7%) advanced SNHL, and 1 (1.9%) patient had profound SNHL according to the pure sound averages of 500, 1000, 2000, and 4000Hz. A significant correlation was found between MPV and PDW levels and the degree of hearing loss during the non-attack period (p<0.05). When verification was performed by regression analysis, the difference in MPV and PDW values was significant (p<0.05) (Figure 3) (Figure 4). There was no significant difference in the other CBC values between groups (p≥0.05) (Table 4).

Table 3: Meniere's group, mean values of neutrophils, lymphocytes, platelets, NLR, PLR, MPV, PDW according to hearing loss during attack period.

Variable	Normal (n=12)	Mild SNHL (n=13)	Medium SNHL (n=25)	Advanced SNHL (n=2)	Profound SNHL (n=2)	p value
Neutrophil count (10^9/L)	4.0±1.0	3.9±1.2	4.8±2.6	3.9±0.6	4.8±3.4	0.749
Lymphocyte count (10^9/L)	2.4 [1.5]	2.4 [1.0]	2.1 [1.3]	1.8 [0.5]	2.7 [0]	0.776
Platelet count (10^3/mm^3)	263±62	269±63	245±48	244±41	219±10	0.656
MPV (fl)	7.6±1.3	8.3±0.8	8.7±1.5	6.9±0.2	7.1±0.4	0.112
PDW (fl)	17.5 [1.3]	17.5 [2.1]	18.9 [1.7]	18.8 [-]	16.9 [-]	0.078
NLR	1.7 [2.1]	1.4 [2.4]	1.7 [0.9]	2.1 [-]	1.6 [-]	0.778
PLR	121±58	109±28	114±34	134±49	84±25	0.395

Continuous variables were presented as mean±standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
PDW: Platelet Distribution Width, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio

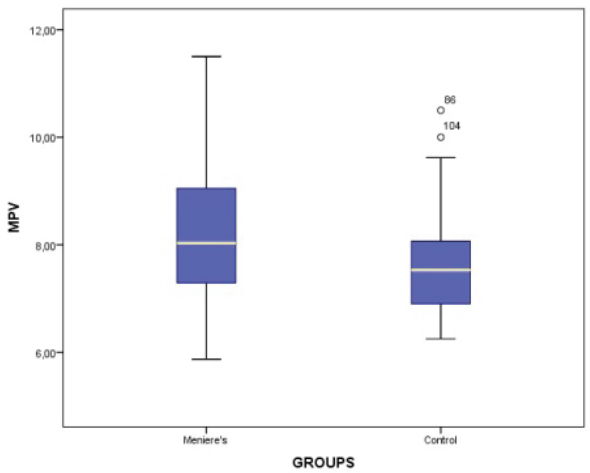

Figure 3: MPV distribution according to the degree of hearing loss in non-attack period.

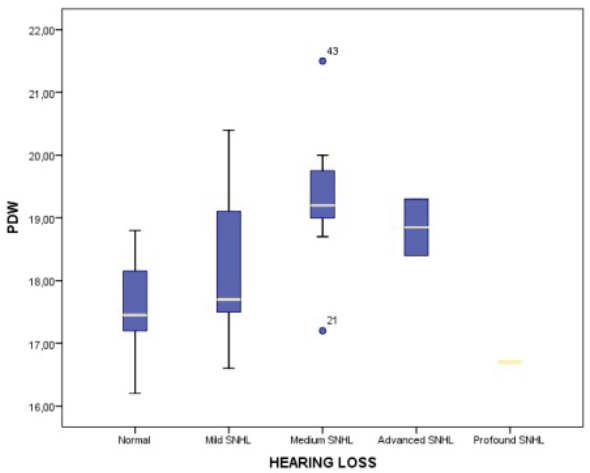

Figure 4: PDW distribution according to the degree of hearing loss in non-attack period.

Table 4: Meniere's group, mean values of neutrophils, lymphocytes, platelets, NLR, PLR, MPV, PDW according to hearing loss during nonattack period.

Variable	Normal (n=20)	Mild SNHL (n=19)	Medium SNHL (n=12)	Advanced SNHL (n=2)	Profound SNHL (n=1)	p value
Neutrophil count (10^9/L)	4.1 [1.8]	3.6 [1.9]	4.2 [2.6]	3.9 [-]	2.3 [-]	0.660
Lymphocyte count (10^9/L)	2.6 [1.4]	2.0 [0.9]	2.3 [1.6]	1.8 [-]	2.0 [-]	0.876
Platelet count (10^3/mm^3)	262±51	253±54	250±61	244±41	212	0.913
MPV (fl)	**7.7±1.2**	**8.1±0.8**	**9.5±1.6**	**6.9±0.2**	**7.4**	**0.004*** **0.002****
PDW (fl)	**17.5±0.7**	**18.0±1.0**	**19.3±1.0**	**18.8±0.6**	**19.7**	**0.001*** **0.014****
NLR	1.6 [2.6]	1.7 [0.7]	1.7 [0.9]	2.1 [1.0]	1.1	0.676
PLR	98 [48]	117 [45]	105 [67]	134 [-]	169	0.668

Continuous variables were presented as mean±standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
MPV: Mean Platelet Volume, PDW: Platelet Distribution Width, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio
*There is a statistically significant difference between MPV and PDW values.
**In the regression analysis, there was a significant difference in MPV and PDW values.

DISCUSSION

Hematologic data were used to evaluate the vascular pathologies that are important in the pathogenesis of MD in the present study. To the best of our knowledge, this is the first study to evaluate complete blood count parameters in MD. MPV and PDW values were significantly high in the Meniere group. In addition, there was a significant correlation between hearing loss and MPV and PDW values in the Meniere group.

The male to female ratio in MD was found to be 1.3/1 in several studies, but in the present study, the ratio was 1/1. (4, 14). Although the course of MD can be highly variable, it usually occurs in the fourth to seventh decade, with episodic vertigo

or sensorineural hearing loss affecting low frequencies. In the present study, the mean age was found to be 48.15±11.917 in accordance with the literature.

Increased PVC venous pressure leads to inadequate drainage of vestibular organs and is one of the important mechanisms in the pathophysiology of MD (10). Friberg et al., in their study, emphasized the classical triad of MD, vertigo, tinnitus, and hearing loss as the only symptom of radiologically detected thrombosis of the sigmoid sinus and jugular bulbus (18). In another study, it was shown that cerebral atherosclerosis, transient ischemic attack, MD, and equilibrium disorders can be seen together with the common etiology of vascular pathology and the underlying mechanism of this status was thought to be due to possible episodic labyrinth ischemia (19).

MPV is a measure of platelet size. Platelets play an important role in initiating atherosclerosis and thrombogenesis (3). Large platelets contain more dense alpha granules, express more adhesion receptors, and have higher thrombotic activity (20). Therefore, MPV is a marker of platelet activation. MPV value is a more specific parameter than platelet count in the evaluation of platelet function (3). MPV is a marker used in systemic inflammatory conditions and cardiovascular pathologies (12). There is a close association between MPV and cardiovascular risk factors such as impaired fasting glucose levels, diabetes mellitus, hypertension, hypercholesterolemia, obesity, and metabolic syndrome (12, 20).

PDW represents heterogeneity in platelet morphology and is clinically associated with platelet activation, such as MPV (21). Increased MPV and PDW reflect increased platelet activation or an increased number of large, hyper aggregated platelets and are considered an independent risk factor for coronary and peripheral arterial disease (13, 14, 22). MPV and PDW values in the present study support vascular pathology. Endler et al. reported that increased MPV and PDW values were independent risk factors for acute myocardial infarction, and other studies have also shown that they are associated with increased mortality and recurrent vascular events after myocardial infarction (23-25).

In a study which examined the CBC results of patients presenting with peripheral vertigo, only NLR values were found to be significant among the other CBC values (26). We were unable to duplicate this result as we did not find a significant difference in NLR values. The reason for this might be due to the low number of patients with MD in our study. In another study comparing CBC values of peripheral vertigo patients with vestibular neuritis, significant results were obtained in NLR, PLR and MPV values (27). The significant results in NLR and PLR values were attributed to inflammatory pathology and the absence of significant results in the present study might indicate that MD is not primarily an inflammatory pathology.

A significant result in MPV value in the present study suggests the important role of the vascular process in MD. Several other researchers examined CBC results in patients with sudden SNHL and tinnitus. In these studies, a significant increase was found in NLR rates, but no significant change was found in MPV values and they associated their results with inflammatory pathology (28,29). In the study in which patients with sudden hearing loss were grouped according to their audiometry grade, it was found that the MPV value was significantly higher in patients with total deafness and in whom all frequencies were affected compared to the control group (30). In the present study, MPV and PDW values showed a correlation with hearing loss in Meniere's patients, suggesting that there may be a correlation between the severity of MD and MPV and PDW values.

CONCLUSION

MPV and PDW values indicate vascular pathologies that are important in the pathogenesis of MD. Our study suggests that MPV and PDW may be potential new markers in evaluating MD, and there may be a significant relationship between MPV and PDW values and disease course and severity. Since the number of patients with advanced and profound SNHL is limited in our study, further studies with MD with advanced hearing loss are required to support our data.

Ethics Committee Approval: Ethics committee approval was obtained from the Local Ethics Committee (Ethics Committee No:71522473/050.01.04/162).

Informed Consent: Written informed consent was obtained.

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