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Postural Stability and Risk of Fall in Vitamin B12 Deficiency

B12 Vitamini Eksikliğinde Postural Stabilite ve Düşme Riski

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ABSTRACT Objective: We aimed to evaluate postural stability and risk of fall in patients with asymptomatic vitamin B12 deficiency. **Material and Methods:** Fifty patients (34 women, 16 men; mean age ± SD: 35±12 years; age range: 18-58 years) who applied to physical medicine and rehabilitation outpatient clinic due to complaints of upper extremity with vitamin B12 deficiency (<200 pq/dl) and without neuropathy according to electromyography results were included in the study. In addition, a total of 49 healthy control subjects (mean age 34±8 years; range 24 to 60 years), 35 females and 14 males with similar age and sex, were included. Gender, age, body mass index (BMI) values and fall history in the last year of the participants were recorded. Fear of falling was evaluated with the Falls Efficacy Scale International (FES-I). With the Tetrax interactive balance system, which is an objective computerized method, posturographic evaluation of the participants was made. In the evaluation of postural stability; the stability index (SI) based on the displacement of the center of gravity and weight distribution index (WDI) on 4 platforms were used. On the other hand, the fall risk results were determined as a numerical value between 0-100. Postural stability and fall risk analyses were evaluated according to the results of the posturographic examination. **Results:** In the patient group, fall history, FES-I score, some SI values and the risk of falling were significantly higher ($p<0.05$). There was no significant relationship between FES-I and gender, age, BMI, and history of fall, while there was a weak negative correlation between some SI values and fall risk ($r=0.03$ and $p<0.05$). However, there was no correlation between the severity of vitamin B12 deficiency and the risk of falling. **Conclusions:** It was found that postural stability is affected, and the risk of fall is increased in patients with asymptomatic vitamin B12 deficiency. This increase in risk of fall was found to be associated with vitamin B12 deficiency but not with the severity of the deficiency.

Keywords: Vitamin B12 deficiency; postural stability; risk of fall

ÖZET Amaç: Asemptomatik B12 vitamini eksikliği olan hastalarda postural stabilite ve düşme riskini değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** Çalışmaya üst ekstremiteye ait şikayetleri nedeniyle fiziksel tıp ve rehabilitasyon polikliniğine başvuran hastalardan, B12 vitamini eksikliği (<200 pq/dl) olan ve elektromiyografi sonuçlarına göre nöropatisi bulunmayan 50 hasta (34 kadın, 16 erkek; ortalama yaş±SS: 35±12 yıl; yaş aralığı: 18-58 yıl) dahil edildi. Ayrıca yaş ve cinsiyetleri benzer olan 49 sağlıklı kontrol bireyi (35 kadın, 14 erkek; ortalama yaş±SS: 34±8 yıl; yaş aralığı: 24-60 yıl) alındı. Katılımcıların cinsiyet, yaş, beden kitle indeksi (BKİ) verileri ve son 1 yıldaki düşme hikâyesi kaydedildi. Düşme korkusu uluslararası düşme etkinliği ölçeği (U-DEÖ) ile değerlendirildi. Objektif bilgisayarlı bir yöntem olan Tetrax interaktif denge sistemi ile, katılımcıların postürografik değerlendirmesi yapıldı. Postural stabilitenin değerlendirilmesinde; ağırlık merkezinin yer değiştirmesi esasına dayanan stabilite indeksi (Sİ) ve 4 platform üzerindeki ağırlık dağılım ölçümleri (ADÖ) kullanıldı. Diğer yandan düşme riski sonuçları ise 0-100 arası sayısal bir değer olarak belirlendi. Postürografik inceleme sonuçlarına göre postüral stabilite ve düşme risk analizi değerlendirildi. **Bulgular:** Hasta grupta düşme hikâyesi, U-DEÖ skoru, bazı Sİ değerleri ve düşme riski anlamlı şekilde daha yüksekti ($p<0,05$). Cinsiyet, yaş, BKİ, düşme hikâyesi ve U-DEÖ değerleri ile düşme riski arasında anlamlı bir ilişki yokken bazı Sİ değerleri ile düşme riski arasında zayıf negatif bir ilişki olduğu bulundu ($r=0,03$ ve $p<0,05$). Ancak B12 vitamini eksikliğinin şiddeti ile düşme riski arasında bir ilişki bulunmadı. **Sonuç:** Çalışmamızda asemptomatik B12 vitamin eksikliği olan hastalarda postural stabilitenin bozulduğu ve düşme riskinin yükseldiği tespit edilmiştir. Düşme riskindeki bu artışın B12 vitamininin eksikliği ile ilişkili olduğu ancak eksikliğin şiddeti ile ilişkili olmadığı anlaşılmıştır.

Anahtar Kelimeler: B12 vitamin eksikliği; postural stabilite; düşme riski

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Vitamin B12 is important in reactions related to DNA, cell metabolism, and B12 deficiency may result in several clinical problems.[1] Peripheral neuropathy due to myelin synthesis defect, degeneration of the cerebrum, posterior and lateral columns of the spinal cord, dizziness, optic atrophy and neurological abnormalities of the autonomic nervous system can be seen in vitamin B12 deficiency.[2-4] The first symptom is symmetrical paresthesia in the hands and feet due to peripheral neuropathy. In addition, signs such as loss of sense of position, vibration and gait ataxia can be seen.[5,6]

In patients with peripheral neuropathy and other neurological symptoms, disorders of sensory and motor functions may result in deterioration of static and dynamic postural stability.[7,8] It is known that B12 deficiency-related neuropathy may impair postural stability and increase the risk of fall.[9] However, to the best of our knowledge, there are no studies about postural stability and risk of fall in patients without neuropathic findings based on electrophysiological assessments. Determination of postural stability, fall risk and associated risk factors in adult patients with asymptomatic vitamin B12 deficiency may contribute to awareness, prevention, and management of falls.

In this study; we aimed to evaluate postural stability and risk of fall by using an objective computerized system in patients with asymptomatic vitamin B12 deficiency.

MATERIAL AND METHODS

This cross-sectional study was conducted between November 2018 and March 2019 at Departments of Physical Medicine and Rehabilitation (PMR) and Neurology at Atatürk University Faculty of Medicine. The study protocol was approved by the Medical Faculty of Atatürk University Ethics Committee (29.11.2018/7;4). Informed consent was obtained from each subject. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The study covered the patients admitted to the PMR outpatient clinic due to problems of the upper extremity, with serum vitamin B12 deficiency (<200 pq/dl). Neurology specialists made electromyography (EMG) evaluations of these patients. According to EMG results, asymptomatic patients without neuropathy were included in the study. Sensory and motor nerve conduction in the upper and lower extremities were evaluated with EMG. In addition, complete blood count, biochemistry tests (blood sugar, liver and kidney function tests, electrolytes), folic acid level and thyroid hormone function tests were normal. There was no patients had the history of drug use and concomitant disease that could affect balance. In the radiological examination of the patients, past radiological data and, if necessary, current radiological data were used. All clinical and radiological examinations were performed by the same PMR and neurology specialists.

Patients who could not tolerate and cooperate during posturographic evaluation test, with a history of spinal, lower extremity and foot problems, cervical and lumbar disc herniation, radicular pain, neuromuscular pathology, limitation of movement, degenerative osteoarthritis, gait pathology, chronic systemic disease, rheumatologic disease, orthopedic or spinal surgery, vertigo, diabetes mellitus, hearing problems, visual problems, circulatory disorders, cognitive impairment and other vitamin deficiencies, who had pathologies that may cause polyneuropathy, and those at old age and with a history of drug use that could increase the risk of falls were excluded from the study. The patient selection for the study protocol is shown in Figure 1.

Falls Efficacy Scale-International (FES-I) is a self-reported questionnaire that assesses the level of concern about falls during daily activities. The reliability and validity of the Turkish version of FES-I were performed by Ulus et al.[10]

Postural stability and fall risk analysis of the patients with vitamin B12 deficiency and the controls were performed by using the Tetrax Interactive Balance System (Sunlight Medical Ltd., Tel Aviv, Israel) with the same technique directed by the user's guide of the device.[11] In the Tetrax system, the posturographic analysis consists of two configurations including detailed equilibrium and drop index evaluations.

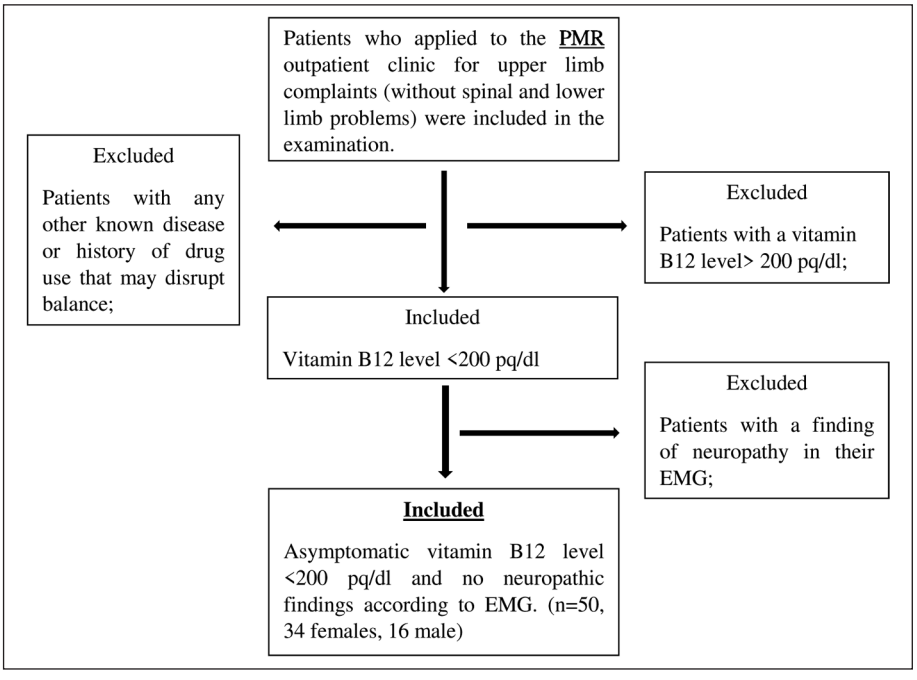

FIGURE 1: Study protocol.

The stability index (SI) based on the evaluation of the displacement of the center of gravity in detailed balance evaluation include Fourier transforms consisting 4 independent wave signals that divided into 8 frequency bands, weight distribution measurements (WDI) on 4 platforms, and synchronization measurements that reflect the effectiveness of coordination of movements between the heels and toes of each foot. It can analyze postural performance by comparing the 4 measurements used for detailed balance in eight different positions. This eight different positions can be listed as follows; eyes open and head straight (NO), eyes closed and head straight (NC), eyes open and while the soles of the feet with sponge head straight (PO), eyes closed and while the soles of the feet with sponge head straight (PC), eyes closed as head right (HR), eyes closed and left rotation (HL), eyes closed as full extension (HB), eyes closed as full flexion (HF). In the study, each of these eight different positions were evaluated in the SI (SI-NO, SI-NC, SI-PO, SI-PC, SI-HR, SI-HL, SI-HB and SI-HF) and WDI (WDI-NO, WDI-NC, WDI-PO, WDI-PC, WDI-HR, WDI-HL, WDI-HB and WDI-HF) parameters.

A falling index derived from the Tetrax balance parameters has been developed to produce a score that will express the patient's risk of fall based on the specific balance factors that affect fall. Fall risk is a numeric value ranging from 0 to 100, with three risk groups, indicating low (0 to 35), moderate (36 to 57), or high (58 to 100) risk of fall.[12]

STATISTICAL ANALYSIS

Minimum sample size required for the study was calculated by using G Power sample size calculator program (v.3.1.9.4) with a Type I error (α) level of 0,05 and Type II error (β) level of 0,05 (power: %95). Effect size was taken as 0,5 since there was no available data in the literature research similar to our study. Therefore, a total of 99 subjects, 50 in patient group, 49 in control group, were included since there might be losses. The analyses were performed by using IBM SPSS 20 statistical analysis program. Data were presented as mean, standard deviation, median, minimum, maximum, percentage, and number. The Kolmogorov-Smirnov test was used to evaluate the normality of data. Independent Samples t-test or Mann Whitney U test were used to compare the groups, depending on the distribution of the samples. Chi-square (2×2) independency test was used to evaluate the relationship between categorical variables. Pearson or Spearman correlation analysis was used

to test correlations between the variables, depending on the distribution of the parameters (r=0.00; no correlation, r=0.01-0.29 range; low level correlation, r=0.30 -0.70; medium level correlation, r=0.71 -0.99; high level correlation, r=1.00; perfect correlation).[13] A p value <0.05 was considered as statistically significant.

RESULTS

Fifty patients (mean age 35.3±11.6 years; range 18 - 58 years) with vitamin B12 deficiency (34 females and 16 males) and 49 healthy individuals (35 females and 14 males) with similar age (mean age 34±8.4 years; range 24 to 60 years) and gender were included in the study. Demographic characteristics of the patients and healthy individuals are summarized in Figure 1. The values were significantly higher in the patient group (p <0.05), while there was no significant difference between patients and healthy individuals in terms of age and gender (p> 0.05).

The history of falls was significantly different between the groups in the last year and six patients with vitamin B12 deficiency had a history of falling for 20 times in the last year (p <0.05). FES-I scores were higher in the patient group and there was a significant difference between the groups (p <0.05). The mean serum B12 vitamin level in the patient group was 151±36 pq/dl, while it was 266 ± 60 pq/dl in the control group and B12 vitamin level was significantly lower in the patient group (p<0.05), (Table 1). In the fall risk analysis evaluated by a computerized system, it was found that the fall risk was significantly higher in the patient group (p<0.05) (Table 1). Overall SI and WDI scores of the postural stability values are shown in eight positions. PC-SI, HL-SI, HB-SI, and HF-SI values were significantly different between the groups (p<0.05), whereas there was no significant difference between the groups in terms of WDI values (p>0.05) (Table 2).

There was no significant relationship between gender, age, BMI, history of fall, FES-I and risk of falls in the patient group (r <0.3 and p>0.05). There was a weak negative correlation between the severity of vitamin B12 deficiency and PC-SI, HL-SI, HB-SI, HF-SI, and PO-WDI postural stability values. However, there was no correlation between the severity of vitamin B12 deficiency and the risk of fall (r<0.3 and p>0.05). While there was a significant positive correlation between all values of SI and fall risk among postural stability values, a significant positive correlation was found only in HR-WDI and HB-WDI amongst WDI values (r<0.03 and p <0.05). In addition, a low level of fall risk was found in the control group and a significant positive correlation was found

TABLE 1: Comparisons of features and fall risk between patients with vitamin B12 deficiency and healthy controls.

	Patients (n=50)	Healthy controls (n=49)	p value
F/M	34/16	35/14	0.711[d]
Mean age ± SD (year)	35±12	34±8	0.623[b]
Mean BMI ± SD (kg/m2)	27.8±4.2	25.3±4.1	0.04*[,b]
Falls history (%)	6 (12)	0	0.013*[,d]
Mean FES-I value ±SD	25.7±9.5	18.6±4.6	0.001**[,b]
Mean B12 level ±SD (pq/dl)	151±36	266±60	0,001*[,b]
Fall risk category			
n (low risk)	19	33	
n (moderate risk)	11	11	
n (high risk)	20	6	
Fall risk assessment; Median (min-max; 0-100)	48 (2-100)	28 (3-100)	0.01*[,c]

n: Number of participants, F: Female, M: Male, SD: Standard deviation, %: Percentage value of the number of person falling in the last 1 year, BMI: Body mass index, FES-I: Falls efficacy scale international, min: Minimum, max: Maximum.

*: p<0.05 was considered as statistically significant between patient and control groups, **: p<0.01 was considered as statistically significant between patient and control groups.

a: The Kolmogorov-Smirnov test, b: Independent samples t-test, c: Mann Whitney U test, d: Chi-square (2×2) independency test, e: Pearson or Spearman correlation.

TABLE 2: Comparisons of SI and WDI values between patients with vitamin B12 deficiency and healthy controls (Mann-Whitney U test).

	Patients (n=50)		Healthy controls (n=49)		
	Median	Min-Max	Median	Min-Max	p value
SI values					
NO-SI	15.3	7.2-29.8	14.6	11-78.7	0.792
NC-SI	22.8	8.8-58.3	19.4	13.1-91.8	0,108
PO-SI	17.6	7.5-38.1	16.7	10-33.3	0.319
PC-SI	26.3€	16.1-51.6	23.6	17-51.9	0.022*
HR-SI	22.4	10.4-42.4	19.7	11.5-49.9	0.056
HL-SI	24.2€	10.7-44.8	19.8	13.8-46.9	0.018*
HB-SI	26.1€	11.3-52.1	21.1	14.4-45.2	0.019*
HF-SI	24.1€	11-59.4	19.2	12.7-37.3	0.014*
WDI values					
NO-WDI	5	1.1-13.5	5.3	1.1-12.5	0.708
NC-WDI	5.1	1.4-14.8	5.7	0.6-14.9	0.988
PO-WDI	8.4	1.5-14.5	6.8	0.9-21.4	0.286
PO-WDI	7.3	0.8-14.6	6.9	1.4-17.1	0.486
HR-WDI	6.4	1.6-16.1	5.1	1.8-14.1	0.273
HL-WDI	5.9	1.1-13.6	4.9	1.8-13.6	0.815
HB-WDI	6.3	1.5-15	5.1	1.2-13.5	0.254
HF-WDI	5.3	1-12.9	5.3	1.4-13	0.851

Min: Minimum, Max: Maximum, SI: Stability Index, WDI: Weight Distribution Index, NO: Open eyes-head neutral, NC: Closed eyes- head neutral,
PO: Open eyes-sponge pad under the feet, PC: Closed eyes-sponge pad under the feet, HR: closed eyes-head rotated to the right, HL: closed eyes-head rotated to the left,
HB: Closed eyes-head fully extended, HF: Closed eyes-head fully flexed,
*: p<0.05 was considered as statistically significant between patient and control groups.

between the fall risk and all SI values except for the NO-SI value ($p < 0.05$) (Table 3).

DISCUSSION

Using an objective computerized method, it was found that postural stability was impaired and the risk of fall was increased in patients with asymptomatic vitamin B12 deficiency. This increase in fall risk was found to be associated with vitamin B12 deficiency but not with the severity of the deficiency. Impaired postural stability and increased risk of falls may have been caused by asymptomatic vitamin B12 deficiency regardless of the factors that we think may be related. Postural stability and balance are complex functions involving various neuromuscular mechanisms. Sensory entry is controlled by sensory evaluation and neuromuscular response. Sensory entry involves the vestibular, visual and proprioceptive systems. An effective motor response requires a steady neuromuscular system and adequate muscle strength.[14]

Vitamin B12 deficiency is one of the most important causes of polyneuropathy and in many studies, it is stated that the amplitude of the sensory nerves is decreased, and motor nerves may also be affected. They also reported that electrophysiological findings may be normal in asymptomatic patients without neuropathic symptoms, while it was also reported that pathological findings can be found in nerve conduction studies.[15,16] As a result of polyneuropathy, superficial and deep sensory losses in proprioceptive and vibration senses can be seen. This sensory loss may cause deterioration in balance and postural stability and consequently increase the risk of falling. However, to our knowledge, there is no study assessing the risk of postural stability and risk of fall by using an objective method in vitamin B12 deficiency patients with normal electrophysiological tests and without neuropathic symptoms.

TABLE 3: The correlation between demographic, clinical, stability index and weight distribution index values with fall risk (Spearman Correlation Test).

	Patients (fall risk)		Healthy controls (fall risk)	
	p	r	p	r
Age (year)	.681	.042	.525	-.093
BMI (kg/m2)	.134	.154	.931	-.013
Falls history	.403	.123	-	-
FES-I	.177	.198	.102	.236
B12 level	.509	-.098	.344	-.138
SI values				
NO-SI	.001**	.680	.060	.270
NC-SI	.001**	.740	.001**	.595
PO-SI	.001**	.819	.039*	.296
PC-SI	.001**	.721	.001**	.469
HR-SI	.001**	.768	.001**	.583
HL-SI	.001**	.801	.001**	.527
HB-SI	.001**	.794	.002**	.433
HF-SI	.001**	.818	.001**	.625
WDI values				
NO-WDI	.346	-.139	.411	-.12
NC-WDI	.326	.145	.221	.178
PO-WDI	.397	.125	.217	-.180
PC-WDI	.724	.052	.623	-.072
HR-WDI	.033*	.309	.416	.119
HL-WDI	.192	.192	.427	.116
HB-WDI	.023*	.327	.441	-.113
HF-WDI	.400	.124	.482	.103

SD: Standard deviation, BMI: Body mass index; FES-I: Falls Efficacy Scale International, SI: Stability Index, WDI: Weight Distribution Index, NO: Open eyes- head neutral, NC: Closed eyes- head neutral, PO: Open eyes-sponge pad under the feet, PC: Closed eyes-sponge pad under the feet, HR: Closed eyes-head rotated to the right, HL: closed eyes-head rotated to the left, HB: Closed eyes-head fully extended, HF: Closed eyes-head fully flexed,
*: Correlation is significant at the 0.05 level, **: Correlation is significant at the 0.01 level.

Risk factors for falls include advanced age (>65 years), female gender, history of falls and fear, living alone, medical problems, physical condition, cognitive dysfunctions, inadequate physical activity and environmental factors.[17] In our study, gender and age groups were similar. The lack of significant relationship with risk of fall may be related with the following factors; patients were asymptomatic and without any neuropathic symptoms, most of the patients were male and mean age was 35 and there were not many elderly patients in the study.

When mean BMI values of the groups were examined, they were found to be overweight. Although BMI values were very close to each other in both groups, a statistically significant difference was found, but we think that this is not clinically important because it does not cause any distress that may pose a risk factor for falls. When mean BMI values of the groups were examined, it was seen that they were overweight (BMI> 25kg/m2). Although BMI values were very close to each other, a statistically significant difference was found. Although it is reported in the literature that there is a significant relationship between high BMI values and postural stability and fall risk, it is also stated that there is no generalization that obese women are at more risk of fall.[18] In our study, we think that this is not clinically important because the patients are not older, BMI values are not very high and they are very close to the control group values.

There was a significant difference in fall history and FES-I values in favor of the patient group in accordance with the literature while there was no correlation between the risk of fall. One of the leading causes of polyneuropathy is peripheral neuropathy due to diabetes mellitus. Many studies have been conducted on balance, postural stability, and fall risk in these patients. It was reported that vibration, touch, and proprioceptive sensory losses occur in diabetic patients with peripheral neuropathy, especially in the lower extremities.[19,20] It was stated that diabetes-related somatosensory system disorders can occur and deteriorated somatosensory system may lead to the improper motor responses, resulting in postural problems, loss of balance and an increased risk of fall, consequently.[14,21-22] In addition, it was stated that loss of balance can also be seen in diabetic patients without neuropathy finding.[23] Therefore, the similarity of the loss of balance in patients with diabetes mellitus without neuropathic findings and the results obtained in our study show that the balance may be affected even in the absence of neuropathic findings. In our study, there was a significant difference between the groups in terms of PC-SI, HL-SI, HB-SI, and HF-SI, but there was no difference in WDI values. In the study, the risk of fall was significantly higher in the patient group and was found to be moderate (48%). However, there was no correlation between the severity of vitamin B12 deficiency and the risk of fall. In addition, a significant positive correlation was found between all SI values and the risk of fall, while only a significant positive correlation was found between HR-WDI and HB-WDI values among WDI values. In our study; SI values were higher in the patient group. This can be considered as a numerical expression of changes in balance parameters of posture disorders, controls, and compensations that cannot be clinically seen.

The higher the SI values the higher the imbalance, while the lower the SI values, the higher the stability and stability. The significant difference in SI values, especially with closed eyes, suggests that sensations such as touch, proprioceptive and vibration, which become dominant when visual perception is eliminated, may be affected even in the asymptomatic period. In addition, the positive relationship between all parameters of SI and the risk of fall may show that the general balance of the person is an important factor affecting the risk of falling. In our study, the second parameter, WDI; asymmetrical distributions between the left and right foot, heels, toe regions, and their cross-interactions are observed. A high WDI means inconsistency of the weight percentage of each on the four-foot platform. High WDI is indicative of a pathology. However, values close to 0 are indicative of maximum standing stability and are often produced by compensating balance mechanisms. In our study, although there was no statistical difference in terms of the WDI values between the groups, WDI was higher in 5 of the 8 values in the patient group compared to the control group. This also indicates that there is too much pathology in the patient group. The difference might be significant if the number of patients was higher or the patients were symptomatic. However, although there was no difference between the groups in terms of WDI values, there was a positive relationship between HB-WDI and HR-WDI values and the risk of falling. These areas are particularly influenced by disorders of the central and peripheral vestibular systems. However, it does not make any clinical sense since there is no need to take any precautions because of the low risk of fall.

In our study, we think that the higher risk of fall seen in patients with asymptomatic vitamin B12 deficiency may be derived from visual, somatosensorial or proprioceptive sensory impulse disorders. In addition, participants' muscle strength, fatigue level at the time of measurement, and other incalculable factors may have an impact on postural stability and thus the risk of falling. Because of this moderate risk of falls, patients with vitamin B12 deficiency should exercise regularly, be careful while walking and running, even if they are asymptomatic. In addition, they should take the necessary measures to prevent slippage when walking or when they are in contact with slippery surfaces. Our study may raise awareness about the increasing incidence of vitamin B12 deficiency and neuropathic symptoms with advancing age, and the prevention of fractures and complications that may occur due to fall with increased degenerative causes and especially osteoporosis in women.

The most important limitation of this study is the possibility of many other factors that are not evaluated in the study but which affect the risk of fall. In addition, the lack of additional two groups as patients with neuropathic symptoms and electrophysiological findings and the patients with neuropathic symptoms without electrophysiological findings and their assessment in terms of postural stability and risk of fall can be listed as the other limitations of our study.

CONCLUSION

In our study, it was found that postural stability is deteriorated and fall risk is increased in patients with asymptomatic vitamin B12 deficiency. This increase in fall risk was found to be associated with vitamin B12 deficiency but not with the severity of the deficiency. The reason for the deterioration in postural stability and increase in the risk of falls in these patients may be caused by impulse disorder from sensory sources. However, further studies with fewer limitations are needed to shed light on the subject.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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